PCT

FORM PTO-1390 (Modified) (REV 5-93) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: 032931-0252

U.S. APPLICATION NO (If known, see 37 C.F.R. 1.5): Unassigned 09/857128

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/CA99/01147	December 1, 1999	December 1, 1998

TITLE OF INVENTION: CHLAMYDIA ANTIGENS AND CORRESPONDING DNA FRAGMENTS AND USES THEREOF

APPLICANT(S) FOR DO/EO/US: Andrew D. MURDIN, Raymond P. OOMEN and Joe WANG

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.

2. ☐ This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.

3. ☐ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).

4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.

5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   - ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
   - ☐ has been transmitted by the International Bureau.
   - ☐ is not required, as the application was filed in the United States Receiving Office (RO/US)

6. ☐ A translation of the International Application into English (35 U.S.C. 371(c)(2)).

7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   - ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   - ☐ have been transmitted by the International Bureau.
   - ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   - ☒ have not been made and will not be made.

8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).

9. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).

10. ☒ A copy of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

11. ☐ Applicant claims small entity status under 37 CFR 1.27 .

Items 12. to 17. below concern other document(s) or information included:

12. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.

13. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.

14. ☒ A FIRST preliminary amendment.
    ☐ A SECOND or SUBSEQUENT preliminary amendment.

15. ☐ A substitute specification.

16. ☐ A change of power of attorney and/or address letter.

17. ☒ Other items or information: A paper copy of the amended sequence listing.

U.S. APPLICATION NO. (If known, see 37 C.F.R. 1.50	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
Unassigned 09/857128	PCT/CA99/01147	032931-0252

18. ☒ The following fees are submitted:	CALCULATIONS	PTO USE ONLY
Basic National Fee (37 CFR 1.492(a)(1)-(5): Search Report has been prepared by the EPO or JPO.....$860.00		
International preliminary examination fee paid to USPTO (37 CFR 1.482).....$690.00		
No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2) $710.00		
Neither international preliminary examination fee (37 CFR 1.482) nor International search fee (37 CFR 1.445(a)(2)) paid to USPTO $1,000.00		
International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4) $100.00		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$860.00	
Surcharge of $130.00 for furnishing the oath or declaration later than 20 Months from the earliest claimed priority date (37 CFR 1.492(e))		

Claims	Number Filed		Included in Basic Fee		Extra Claims		Rate		
Total Claims	39	-	20	=	19	×	$18.00	$342.00	
Independent Claims	11	-	3	=	8	×	$80.00	$640.00	
Multiple dependent claim(s) (if applicable)							$270.00		
TOTAL OF ABOVE CALCULATIONS =								$1842.00	
Reduction by ½ for filing by small entity, if applicable.								$0.00	
SUBTOTAL =								$1842.00	
Processing fee of $130.00 for furnishing English translation later the 20 months from the earliest claimed priority date (37 CFR 1.492(f). +									
TOTAL NATIONAL FEE =								$1842.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). $40.00 per property +									
TOTAL FEES ENCLOSED =								$1842.00	
							Amount to be: refunded	$	
							charged	$	

a. ☒ A check in the amount of $1842.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. 19-0741 in the amount of $.00 to the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 19-0741. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Foley & Lardner
Washington Harbour
3000 K Street, N.W., Suite 500
Washington, D.C. 20007-5109

Michele M Simkin

SIGNATURE

NAME MICHELE M. SIMKIN

REGISTRATION NUMBER 34,717

FORM PTO-1390 (Modified) (REV 5-93) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: 032931-0252

		U.S APPLICATION NO. (If known, see 37 C.F.R. 1.5) Unassigned 09/857128
INTERNATIONAL APPLICATION NO. PCT/CA99/01147	INTERNATIONAL FILING DATE December 1, 1999	PRIORITY DATE CLAIMED December 1, 1998

TITLE OF INVENTION
CHLAMYDIA ANTIGENS AND CORRESPONDING DNA FRAGMENTS AND USES THEREOF

APPLICANT(S) FOR DO/EO/US
Andrew D. MURDIN, Raymond P. OOMEN and Joe WANG

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3. ☐ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).

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   - ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
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   - ☐ have not been made; however, the time limit for making such amendments has NOT expired.
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17. ☒ Other items or information: A paper copy of the amended sequence listing.

U.S. APPLICATION NO. (If known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
Unassigned 09/857128	PCT/CA99/01147	032931-0252

18. ☒ The following fees are submitted:	CALCULATIONS	PTO USE ONLY
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International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4).....$100.00		
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Foley & Lardner
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3000 K Street, N.W., Suite 500
Washington, D.C. 20007-5109

Michele M Simkin

SIGNATURE

NAME MICHELE M. SIMKIN

REGISTRATION NUMBER 34,717

Atty. Dkt. No. 032931-0252

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Andrew D. MURDIN et al.

Title: CHLAMYDIA ANTIGENS AND CORRESPONDING DNA FRAGMENTS AND USES THEREOF

Appl. No.: Unassigned

Filing Date: 06/01/2001

Examiner: Unassigned

Art Unit: Unassigned

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

In accordance with 37 CFR §1.121, please substitute for original claims 3, 7, 12-16, 20, 25, 31-34 and 36-39 the following rewritten versions of the same claims, as amended. The changes are shown explicitly in the attached "Version with Markings to Show Changes Made."

IN THE CLAIMS:

3. (Amended) A nucleic acid molecule comprising a nucleic acid sequence which is anti-sense to the nucleic acid molecule of claim 1.

7. (Amended) A nucleic acid molecule according to claim 1, operatively linked to one or more expression control sequences.

8. (Amended) A vaccine comprising a vaccine vector and at least one first nucleic acid selected from any of:

(i) SEQ ID Nos: 1 to 10;

(ii) a nucleic acid sequence which encodes a polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(iii) a nucleic acid sequence comprising at least 38 consecutive nucleotides from any one of the nucleic acid sequences of (i) and (ii);

(iv) a nucleic acid sequence which encodes a polypeptide which is at least 75% identical in amino acid sequence to the polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(v) a nucleic acid sequence which encodes a polypeptide whose sequence is set forth in any one of SEQ ID Nos: 11 to 16;

(vi) a nucleic acid sequence which encodes an immunogenic fragment comprising at least 12 consecutive amino acids from any one of SEQ ID Nos: 11 to 16; and

(vii) a nucleic acid sequence which encodes a polypeptide as defined in (i) to (v) or an immunogenic fragment as defined in (vi) which has been modified without loss of immunogenicity, wherein said modified polypeptide or fragment is at least 75% identical in amino acid sequence to the corresponding polypeptide of (i) to (v) or the corresponding fragment of (vi);

wherein each first nucleic acid is capable of being expressed.

9. (Amended) A vaccine comprising a vaccine vector and at least one first nucleic acid encoding a fusion protein, wherein the fusion protein comprises:

(a) a first polypeptide selected from any of:

(i) a polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(ii) a polypeptide encoded by a nucleic acid sequence comprising at least 38 consecutive nucleotides from any one of SEQ ID Nos: 1 to 10;

(iii) a polypeptide which is at least 75% identical in amino acid sequence to the polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(iv) a polypeptide whose sequence is set forth in any one of SEQ ID Nos: 11 to 16;

(v) an immunogenic fragment comprising at least 12 consecutive amino acids from any one of SEQ ID Nos: 11 to 16; and

(vi) a polypeptide as defined in (i) to (iv) or an immunogenic fragment as defined in (v) which has been modified without loss of immunogenicity, wherein said modified polypeptide or fragment is at least 75% identical in amino acid sequence to the corresponding polypeptide of (i) to (iv) or the corresponding fragment of (v); and

(b) a second polypeptide;

wherein each first nucleic acid is capable of being expressed.

12. (Amended) The vaccine of claim 8 wherein each first nucleic acid is operatively linked to one or more expression control sequences.

13. (Amended) A vaccine according to claim 8 wherein each first nucleic acid is expressed as a polypeptide,

and wherein the vaccine comprises a second nucleic acid encoding an additional polypeptide which enhances the immune response to the polypeptide expressed by the first nucleic acid.

14. (Amended) The vaccine of claim 13 wherein the second nucleic acid encodes an additional *Chlamydia* polypeptide.

15. (Amended) A pharmaceutical composition comprising a nucleic acid according to claim 1 and a pharmaceutically acceptable carrier.

16. (Amended) A pharmaceutical composition comprising a vaccine according to claim 8 and a pharmaceutically acceptable carrier.

20. (Amended) A polypeptide encoded by a nucleic acid sequence according to claim 2.

25. (Amended) A method for producing a polypeptide of claim 20, comprising the step of culturing a unicellular host transformed with a nucleic acid encoding a polypeptide of claim 20.

26. (Amended) An antibody against the polypeptide of claim 20.

27. (Amended) A vaccine comprising at least one first polypeptide selected from any of:

(i) a polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(ii) a polypeptide encoded by a nucleic acid sequence comprising at least 38 consecutive nucleotides from any one of SEQ ID Nos: 1 to 10;

(iii) a polypeptide which is at least 75% identical in amino acid sequence to the polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(iv) a polypeptide whose sequence is set forth in any one of SEQ ID Nos: 11 to 16;

(v) an immunogenic fragment comprising at least 12 consecutive amino acids from any one of SEQ ID Nos: 11 to 16; and

(vi) a polypeptide as defined in (i) to (iv) or an immunogenic fragment as defined in (v) which has been modified without loss of immunogenicity, wherein said modified polypeptide or fragment is at least 75% identical in amino acid sequence to the corresponding polypeptide of (i) to (iv) or the corresponding fragment of (v).

28. (Amended) A vaccine comprising at least one fusion protein, wherein the fusion protein comprises:

(a) a first polypeptide selected from any of:

(i) a polypeptide encoded by SEQ ID No: 1;

(ii) a polypeptide encoded by a nucleic acid sequence comprising at least 38 consecutive nucleotides from SEQ ID No: 1;

(iii) a polypeptide which is at least 75% identical in amino acid sequence to the polypeptide encoded by SEQ ID No: 1;

(iv) a polypeptide whose sequence is set forth in SEQ ID No: 2;

(v) an immunogenic fragment comprising at least 12 consecutive amino acids from SEQ ID No:2; and

(vi) a polypeptide as defined in (i) to (iv) or an immunogenic fragment as defined in (v) which has been modified without loss of immunogenicity, wherein said modified polypeptide or fragment is at least 75% identical in amino acid sequence to the corresponding polypeptide of (i) to (iv) or the corresponding fragment of (v); and

(b) a second polypeptide.

31. (Amended) A vaccine comprising at least one first polypeptide according to claim 20 and an additional polypeptide which enhances the immune response to the first polypeptide.

32. (Amended) The vaccine of claim 31 wherein the additional polypeptide comprises a *Chlamydia* polypeptide.

33. (Amended) A pharmaceutical composition comprising a polypeptide according to claim 20 and a pharmaceutically acceptable carrier.

34. (Amended) A pharmaceutical composition comprising a vaccine according to claim 27 and a pharmaceutically acceptable carrier.

36. (Amended) A method for preventing or treating *Chlamydia* infection comprising administering to a patient an effective amount of:

(a) a nucleic acid according to claim 2;

(b) a vaccine comprising a vaccine vector and at least one first nucleic acid according to claim 2;

(c) a pharmaceutical composition comprising a nucleic acid according to claim 2 and a pharmaceutically acceptable carrier;

(d) a polypeptide encoded by a nucleic acid according to claim 2; or

(e) an antibody against a polypeptide encoded by a nucleic acid according to claim 2.

37. (Amended) A method of detecting *Chlamydia* infection comprising the step of contacting a body fluid of a mammal to be tested, with a component selected from any one of:

(a) a nucleic acid according to claim 2;

(b) a polypeptide encoded by a nucleic acid according to claim 2; and

(c) an antibody against a polypeptide encoded by a nucleic acid according to claim 2.

38. (Amended) A diagnostic kit comprising instructions for use and a component selected from any one of:

(a) a nucleic acid according to claim 2;

(b) a polypeptide encoded by a nucleic acid according to claim 2; and

(c) an antibody against a polypeptide encoded by a nucleic acid according to claim 2.

39. (Amended) A method for identifying a polypeptide of claim 20 which induces an immune response effective to prevent or lessen the severity of *Chlamydia* infection in a mammal previously immunized with polypeptide, comprising the steps of:

(a) immunizing a mouse with the polypeptide of claim 20; and

(b) inoculating the immunized mouse with *Chlamydia;*

wherein the polypeptide which prevents or lessens the severity of *Chlamydia* infection in the immunized mouse compared to a non-immunized control mouse is identified.

REMARKS

Applicant respectfully request that the foregoing amendments to Claims 3, 7, 12-16, 20, 25, 31-34 and 36-39 be entered in order to avoid this application incurring a surcharge for the presence of one or more multiple dependent claims.

Respectfully submitted,

Date June 1, 2001 By Michele M. Simkin

FOLEY & LARDNER
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Michele M. Simkin
Attorney for Applicant
Registration No. 34,717

VERSION WITH MARKINGS TO SHOW CHANGES MADE

3. (Amended) A nucleic acid molecule comprising a nucleic acid sequence which is anti-sense to the nucleic acid molecule of claim 1 [or 2].

7. (Amended) A nucleic acid molecule according to [any one of claims 1 to 6] claim 1, operatively linked to one or more expression control sequences.

8. (Amended) A vaccine comprising a vaccine vector and at least one first nucleic acid selected from any of:

(i) SEQ ID Nos: 1 to 10;

(ii) a nucleic acid sequence which encodes a polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(iii) a nucleic acid sequence comprising at least 38 consecutive nucleotides from any one of the nucleic acid sequences of (i) and (ii);

(iv) a nucleic acid sequence which encodes a polypeptide which is at least 75% identical in amino acid sequence to the polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(v) a nucleic acid sequence which encodes a polypeptide whose sequence is set forth in any one of SEQ ID Nos: 11 to 16;

(vi) a nucleic acid sequence which encodes an immunogenic fragment comprising at least 12 consecutive amino acids from any one of SEQ ID Nos: 11 to 16; and

(vii) a nucleic acid sequence which encodes a polypeptide as defined in (i) to (v) or an immunogenic fragment as defined in (vi) which has been modified without loss of immunogenicity, wherein said modified polypeptide or fragment is at least 75% identical in amino acid sequence to the corresponding polypeptide of (i) to (v) or the corresponding fragment of (vi);

wherein each first nucleic acid is capable of being expressed [and wherein the vaccine optionally comprises a second nucleic acid encoding and capable of expressing an additional polypeptide which enhances the immune response to the polypeptide expressed by the first nucleic acid].

9. (Amended) A vaccine comprising a vaccine vector and at least one first nucleic acid encoding a fusion protein, wherein the fusion protein comprises:

(a) a first polypeptide selected from any of:

(i) a polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(ii) a polypeptide encoded by a nucleic acid sequence comprising at least 38 consecutive nucleotides from any one of SEQ ID Nos: 1 to 10;

(iii) a polypeptide which is at least 75% identical in amino acid sequence to the polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(iv) a polypeptide whose sequence is set forth in any one of SEQ ID Nos: 11 to 16;

(v) an immunogenic fragment comprising at least 12 consecutive amino acids from any one of SEQ ID Nos: 11 to 16; and

(vi) a polypeptide as defined in (i) to (iv) or an immunogenic fragment as defined in (v) which has been modified without loss of immunogenicity, wherein said modified polypeptide or fragment is at least 75% identical in amino acid sequence to the corresponding polypeptide of (i) to (iv) or the corresponding fragment of (v); and

(b) a second polypeptide;

wherein each first nucleic acid is capable of being expressed [and wherein the vaccine optionally comprises a second nucleic acid encoding and capable of expressing an additional polypeptide which enhances the immune response to the first polypeptide].

12. (Amended) The vaccine of [any one of claims 8 to 11] claim 8 wherein each first nucleic acid is operatively linked to one or more expression control sequences.

13. (Amended) A vaccine [comprising at least one first nucleic acid] according to [any one of claims 1, 2, and 4 to 7 and a vaccine vector] claim 8 wherein each first nucleic acid is expressed as a polypeptide, and wherein the vaccine [optionally comprising] comprises a second nucleic acid encoding an additional polypeptide which enhances the immune response to the polypeptide expressed by [said] the first nucleic acid.

14. (Amended) The vaccine of [any one of claims 8 to 13] claim 13 wherein the second nucleic acid encodes an additional *Chlamydia* polypeptide.

15. (Amended) A pharmaceutical composition comprising a nucleic acid according to [any one of claims 1 to 7] claim 1 and a pharmaceutically acceptable carrier.

16. (Amended) A pharmaceutical composition comprising a vaccine according to [any one of claims 8 to 14] claim 8 and a pharmaceutically acceptable carrier.

20. (Amended) A polypeptide encoded by a nucleic acid sequence according to [any one of claims 1, 2 and 4 to 7] claim 2.

25. (Amended) A method for producing a polypeptide of claim 20, [or 21, or a fusion protein of any one of claims 22 to 24] comprising the step of culturing a unicellular host [of claim 17] transformed with a nucleic acid encoding a polypeptide of claim 20.

26. (Amended) An antibody against the polypeptide of claim 20 [or 21, or against a fusion protein of any one of claims 22 to 24].

27. (Amended) A vaccine comprising at least one first polypeptide selected from any of:

(i) a polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(ii) a polypeptide encoded by a nucleic acid sequence comprising at least 38 consecutive nucleotides from any one of SEQ ID Nos: 1 to 10;

(iii) a polypeptide which is at least 75% identical in amino acid sequence to the polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(iv) a polypeptide whose sequence is set forth in any one of SEQ ID Nos: 11 to 16;

(v) an immunogenic fragment comprising at least 12 consecutive amino acids from any one of SEQ ID Nos: 11 to 16; and

(vi) a polypeptide as defined in (i) to (iv) or an immunogenic fragment as defined in (v) which has been modified without loss of immunogenicity, wherein said modified polypeptide or fragment is at least 75% identical in amino acid sequence to the corresponding polypeptide of (i) to (iv) or the corresponding fragment of (v)[:

wherein the vaccine optionally comprises an additional polypeptide which enhances the immune response to the first polypeptide].

28. (Amended) A vaccine comprising at least one fusion protein, wherein the fusion protein comprises:

(a) a first polypeptide selected from any of:

(i) a polypeptide encoded by SEQ ID No: 1;

(ii) a polypeptide encoded by a nucleic acid sequence comprising at least 38 consecutive nucleotides from SEQ ID No: 1;

(iii) a polypeptide which is at least 75% identical in amino acid sequence to the polypeptide encoded by SEQ ID No: 1;

(iv) a polypeptide whose sequence is set forth in SEQ ID No: 2;

(v) an immunogenic fragment comprising at least 12 consecutive amino acids from SEQ ID No:2; and

(vi) a polypeptide as defined in (i) to (iv) or an immunogenic fragment as defined in (v) which has been

modified without loss of immunogenicity, wherein said modified polypeptide or fragment is at least 75% identical in amino acid sequence to the corresponding polypeptide of (i) to (iv) or the corresponding fragment of (v); and

(b) a second polypeptide [:

wherein the vaccine optionally comprises an additional polypeptide which enhances the immune response to the first polypeptide].

31. (Amended) A vaccine comprising at least one first polypeptide according to [any one of claims 20 to 24, optionally comprising] claim 20 and an additional polypeptide which enhances the immune response to the first polypeptide.

32. (Amended) The vaccine of [any one of claims 27 to 31] claim 31 wherein the additional polypeptide comprises a *Chlamydia* polypeptide.

33. (Amended) A pharmaceutical composition comprising a polypeptide according to [any one of claims 20 to 24] claim 20 and a pharmaceutically acceptable carrier.

34. (Amended) A pharmaceutical composition comprising a vaccine according to [any one of claims 27 to 32] claim 27 and a pharmaceutically acceptable carrier.

36. (Amended) A method for preventing or treating *Chlamydia* infection [using] comprising administering to a patient an effective amount of:

(a) [the] a nucleic acid [of any one of claims 1 to 7] according to claim 2;

(b) [the vaccine of any one of claims 8 to 14 and 27 to 32] a vaccine comprising a vaccine vector and at least one first nucleic acid according to claim 2;

(c) [the] a pharmaceutical composition [of any one of claims 15, 16, and 33 to 35] comprising a nucleic acid according to claim 2 and a pharmaceutically acceptable carrier;

(d) [the] a polypeptide [of claim 20 or 21, or a fusion protein of any one of claims 22 to 24] encoded by a nucleic acid according to claim 2; or

(e) [the] an antibody [of claim 26] against a polypeptide encoded by a nucleic acid according to claim 2.

37. (Amended) A method of detecting *Chlamydia* infection comprising the step of [assaying] contacting a body fluid of a mammal to be tested, with a component selected from any one of:

(a) [the] a nucleic acid [of any one of claims 1 to 7] according to claim 2;

(b) [the] a polypeptide [of claim 20 or 21, or a fusion protein of any one of claims 22 to 24] encoded by a nucleic acid according to claim 2; and

(c) [the] an antibody [of claim 26] against a polypeptide encoded by a nucleic acid according to claim 2.

38. (Amended) A diagnostic kit comprising instructions for use and a component selected from any one of:

(a) [the] a nucleic acid [of any one of claims 1 to 7] according to claim 2;

(b) [the] a polypeptide [of claim 20 or 21, or a fusion protein of any one of claims 22 to 24] encoded by a nucleic acid according to claim 2; and

(c) [the] an antibody [of claim 26] against a polypeptide encoded by a nucleic acid according to claim 2.

39. (Amended) A method for identifying a polypeptide of claim 20 [or 21, or a fusion protein of any one of claims 22 to 24] which induces an immune response effective to prevent or lessen the severity of *Chlamydia* infection in a mammal previously immunized with polypeptide, comprising the steps of:

(a) immunizing a mouse with the polypeptide [or fusion protein] of claim 20; and

(b) inoculating the immunized mouse with *Chlamydia;*

wherein the polypeptide [or fusion protein] which prevents or lessens the severity of *Chlamydia* infection in the immunized mouse compared to a non-immunized control mouse is identified.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Andrew D. MURDIN et al.

Title: CHLAMYDIA ANTIGENS AND CORRESPONDING DNA FRAGMENTS AND USES THEREOF

Appl. No.: 09/857,128

Filing Date: September 20, 2001

Examiner: Unassigned

Art Unit: Unassigned

PRELIMINARY AMENDMENT

Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

Prior to examination of the above-identified application, Applicants respectfully request that the following amendments be entered into the application:

IN THE SPECIFICATION:

On Page 7, lines 11 and 12, please delete:

[Knudsen et al (1996) Third Meeting of the European Society for Chlamydia Research, Vienna).]

and replace with the following:

Gaydos et al (1992) Infection and Immunity. 60 (12): 5319-5323).

REMARKS

Applicants respectfully request that the foregoing amendments be entered.

Respectfully submitted,

Date September 20, 2001

By [signature]

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TITLE OF INVENTION

CHLAMYDIA ANTIGENS AND CORRESPONDING DNA FRAGMENTS AND USES THEREOF

REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application No. 60/110,427, filed December 1, 1998, U.S. Provisional Application No.60/110,438, filed December 1, 1998,U.S. Provisional Application No. 60/110,339, filed December 1, 1998, U.S. Provisional Application No. 60/110,428, filed December 1, 1998, U.S. Provisional Application No. 60/110,340, filed December 1, 1998.

FIELD OF INVENTION

The present invention relates to *Chlamydia* antigens and corresponding DNA molecules, which can be used to prevent and treat *Chlamydia* infection in mammals, such as humans.

BACKGROUND OF THE INVENTION

Chlamydiae are prokaryotes. They exhibit morphologic and structural similarities to gram-negative bacteria including a trilaminar outer membrane, which contains lipopolysaccharide and several membrane proteins that are structurally and functionally analogous to proteins found in *E coli*. They are obligate intra-cellular parasites with a unique biphasic life cycle consisting of a metabolically inactive but infectious extracellular stage and a replicating but non-infectious intracellular stage. The replicative stage of the life-cycle takes place within a membrane-bound inclusion which sequesters the bacteria away from the cytoplasm of the infected host cell.

C. pneumoniae is a common human pathogen, originally described as the TWAR strain of *Chlamydia psittaci* but subsequently recognised to be a new species. *C. pneumoniae* is antigenically, genetically and morphologically distinct from

other chlamydia species (*C. trachomatis, C. pecorum* and *C. psittaci*). It shows 10% or less DNA sequence homology with either of *C. trachomatis* or *C. psittaci*.

C. pneumoniae is a common cause of community acquired pneumonia, only less frequent than *Streptococcus pneumoniae* and *Mycoplasma pneumoniae* (Grayston *et al.* (1995) Journal of Infectious Diseases 168:1231; Campos *et al.* (1995) Investigation of Ophthalmology and Visual Science 36:1477). It can also cause upper respiratory tract symptoms and disease, including bronchitis and sinusitis (Grayston *et al.* (1995) Journal of Infectious Diseases 168:1231; Grayston *et al* (1990) Journal of Infectious Diseases 161:618; Marrie (1993) Clinical Infectious Diseases. 18:501; Wang *et al* (1986) Chlamydial infections). Cambridge University Press, Cambridge. p. 329The great majority of the adult population (over 60%) has antibodies to *C. pneumoniae* (Wang *et al* (1986) Chlamydial infections. Cambridge University Press, Cambridge. p. 329), indicating past infection which was unrecognized or asymptomatic.

C. pneumoniae infection usually presents as an acute respiratory disease (*i.e.*, cough, sore throat, hoarseness, and fever; abnormal chest sounds on auscultation). For most patients, the cough persists for 2 to 6 weeks, and recovery is slow. In approximately 10% of these cases, upper respiratory tract infection is followed by bronchitis or pneumonia. Furthermore, during a *C. pneumoniae* epidemic, subsequent co-infection with pneumococcus has been noted in about half of these pneumonia patients, particularly in the infirm and the elderly. As noted above, there is more and more evidence that *C. pneumoniae* infection is also linked to diseases other than respiratory infections.

The reservoir for the organism is presumably people. In contrast to *C. psittaci* infections, there is no known bird or animal reservoir. Transmission has not been clearly defined. It may result from direct contact with secretions, from fomites,

or from airborne spread. There is a long incubation period, which may last for many months. Based on analysis of epidemics, *C. pneumoniae* appears to spread slowly through a population (case-to-case interval averaging 30 days) because infected persons are inefficient transmitters of the organism. Susceptibility to *C. pneumoniae* is universal. Reinfections occur during adulthood, following the primary infection as a child. *C. pneumoniae* appears to be an endemic disease throughout the world, noteworthy for superimposed intervals of increased incidence (epidemics) that persist for 2 to 3 years. *C. trachomatis* infection does not confer cross-immunity to *C. pneumoniae*. Infections are easily treated with oral antibiotics, tetracycline or erythromycin (2 g/d, for at least 10 to 14 d). A recently developed drug, azithromycin, is highly effective as a single-dose therapy against chlamydial infections.

In most instances, *C. pneumoniae* infection is often mild and without complications, and up to 90% of infections are subacute or unrecognized. Among children in industrialized countries, infections have been thought to be rare up to the age of 5 y, although a recent study (E Normann *et al*, Chlamydia pneumoniae in children with acute respiratory tract infections, Acta Paediatrica, 1998, Vol 87, Iss 1, pp 23-27) has reported that many children in this age group show PCR evidence of infection despite being seronegative, and estimates a prevalence of 17-19% in 2-4 y olds. In developing countries, the seroprevalence of *C. pneumoniae* antibodies among young children is elevated, and there are suspicions that *C. pneumoniae* may be an important cause of acute lower respiratory tract disease and mortality for infants and children in tropical regions of the world.

From seroprevalence studies and studies of local epidemics, the initial *C. pneumoniae* infection usually happens between the ages of 5 and 20 y. In the USA, for example, there

are estimated to be 30,000 cases of childhood pneumonia each year caused by *C. pneumoniae*. Infections may cluster among groups of children or young adults (*e.g.*, school pupils or military conscripts).

C. pneumoniae causes 10 to 25% of community-acquired lower respiratory tract infections (as reported from Sweden, Italy, Finland, and the USA). During an epidemic, *C. pneumonia* infection may account for 50 to 60% of the cases of pneumonia. During these periods, also, more episodes of mixed infections with *S. pneumoniae* have been reported.

Reinfection during adulthood is common; the clinical presentation tends to be milder. Based on population seroprevalence studies, there tends to be increased exposure with age, which is particularly evident among men. Some investigators have speculated that a persistent, asymptomatic *C. pneumoniae* infection state is common.

In adults of middle age or older, *C. pneumoniae* infection may progress to chronic bronchitis and sinusitis. A study in the USA revealed that the incidence of pneumonia caused by *C. pneumoniae* in persons younger than 60 years is 1 case per 1,000 persons per year; but in the elderly, the disease incidence rose three-fold. *C. pneumoniae* infection rarely leads to hospitalization, except in patients with an underlying illness.

Of considerable importance is the association of atherosclerosis and *C. pneumoniae* infection. There are several epidemiological studies showing a correlation of previous infections with *C. pneumoniae* and heart attacks, coronary artery and carotid artery disease (Saikku *et al.*(1988) Lancet; ii:983; Thom *et al.* (1992) JAMA 268:68; Linnanmaki *et al.* (1993), Circulation 87:1030; Saikku *et al.* (1992) Annals Internal Medicine 116:273; Melnick *et al* (1993) American Journal of Medicine 95:499). Moreover, the organisms has been detected in atheromas and fatty streaks of the coronary, carotid, peripheral

arteries and aorta (Shor *et al.* (1992) South African. Medical Journal 82:158; Kuo *et al.* (1993) Journal of Infectious Diseases 167:841; Kuo *et al.* (1993) Arteriosclerosis and Thrombosis 13:1500; Campbell *et al* (1995) Journal of Infectious Diseases 172:585; Chiu *et al.* Circulation, 1997 (In Press)). Viable *C. pneumoniae* has been recovered from the coronary and carotid artery (Ramirez *et al* (1996) Annals of Internal Medicine 125:979; Jackson *et al.* Abst. K121, p272, 36th ICAAC, 15-18 Sept. 1996, New Orleans). Furthermore, it has been shown that *C. pneumoniae* can induce changes of atherosclerosis in a rabbit model (Fong *et al* (1997) Journal of Clinical Microbiolology 35:48). Taken together, these results indicate that it is highly probable that *C. pneumoniae* can cause atherosclerosis in humans, though the epidemiological importance of chlamydial atherosclerosis remains to be demonstrated.

A number of recent studies have also indicated an association between *C. pneumoniae* infection and asthma. Infection has been linked to wheezing, asthmatic bronchitis, adult-onset asthma and acute exacerbations of asthma in adults, and small-scale studies have shown that prolonged antibiotic treatment was effective at greatly reducing the severity of the disease in some individuals (Hahn DL, *et al.* Evidence for Chlamydia pneumoniae infection in steroid-dependent asthma. Ann Allergy Asthma Immunol. 1998 Jan; 80(1): 45-49.; Hahn DL, *et al.* Association of Chlamydia pneumoniae IgA antibodies with recently symptomatic asthma. Epidemiol Infect. 1996 Dec; 117(3): 513-517; Bjornsson E, *et al.* Serology of chlamydia in relation to asthma and bronchial hyperresponsiveness. Scand J Infect Dis. 1996; 28(1): 63-69.; Hahn DL. Treatment of *Chlamydia pneumoniae* infection in adult asthma: a before-after trial. J Fam Pract. 1995 Oct; 41(4): 345-351.; Allegra L, *et al.* Acute exacerbations of asthma in adults: role of Chlamydia pneumoniae infection. Eur Respir J. 1994 Dec; 7(12): 2165-2168.; Hahn DL, *et al.* Association of Chlamydia pneumoniae (strain TWAR)

infection with wheezing, asthmatic bronchitis, and adult-onset asthma. JAMA. 1991 Jul 10; 266(2): 225-230).

In light of these results a protective vaccine against *C. pneumoniae* infection would be of considerable importance. There is not yet an effective vaccine for any human chlamydial infection. It is conceivable that an effective vaccine can be developed using physically or chemically inactivated Chlamydiae. However, such a vaccine does not have a high margin of safety. In general, safer vaccines are made by genetically manipulating the organism by attenuation or by recombinant means. Accordingly, a major obstacle in creating an effective and safe vaccine against human chlamydial infection has been the paucity of genetic information regarding Chlamydia, specifically *C. pneumoniae*.

Studies with *C. trachomatis* and *C. psittaci* indicate that safe and effective vaccine against Chlamydia is an attainable goal. For example, mice which have recovered from a lung infection with *C. trachomatis* are protected from infertility induced by a subsequent vaginal challenge (Pal *et al.*(1996) Infection and Immunity.64:5341). Similarly, sheep immunized with inactivated *C. psittaci* were protected from subsequent chlamydial-induced abortions and stillbirths (Jones *et al.* (1995) Vaccine 13:715). Protection from chlamydial infections has been associated with Th1 immune responses, particularly the induction of INFg - producing CD4+T-cells (Igietsemes *et al.* (1993) Immunology 5:317). The adoptive transfer of CD4+ cell lines or clones to nude or SCID mice conferred protection from challenge or cleared chronic disease (Igietseme *et al* (1993) Regional Immunology 5:317; Magee *et al* (1993) Regional Immunology 5: 305), and *in vivo* depletion of CD4+ T cells exacerbated disease post-challenge (Landers *et al* (1991) Infection & Immunity 59:3774; Magee *et al* (1995) Infection & Immunity 63:516). However, the presence of sufficiently high titres of neutralising antibody at mucosal

surfaces can also exert a protective effect (Cotter *et al.* (1995) Infection and Immunity 63:4704).

Antigenic variation within the species *C. pneumoniae* is not well documented due to insufficient genetic information, though variation is expected to exist based on *C. trachomatis*. Serovars of *C. trachomatis* are defined on the basis of antigenic variation in the major outer membrane protein (MOMP), but published *C. pneumoniae* MOMP gene sequences show no variation between several diverse isolates of the organism (Campbell *et al* (1990) Infection and Immunity 58:93; McCafferty *et al* (1995) Infection and Immunity 63:2387-9; Knudsen *et al* (1996) Third Meeting of the European Society for Chlamydia Research, Vienna). Regions of the protein known to be conserved in other chlamydial MOMPs are conserved in *C. pneumoniae* (Campbell *et al* (1990) Infection and Immunity 58:93; McCafferty *et al* (1995) Infection and Immunity 63:2387-9). One study has described a strain of *C. pneumoniae* with a MOMP of greater that usual molecular weight, but the gene for this has not been sequenced (Grayston *et al.* (1995) Journal of Infectious Diseases 168:1231). Partial sequences of outer membrane protein 2 from nine diverse isolates were also found to be invariant (Ramirez *et al* (1996) Annals of Internal Medicine 125:979). The genes for HSP60 and HSP70 show little variation from other chlamydial species, as would be expected. The gene encoding a 76kDa antigen has been cloned from a single strain of *C. pneumoniae*. It has no significant similarity with other known chlamydial genes (Marrie (1993) Clinical Infectious Diseases. 18:501).

Many antigens recognised by immune sera to *C. pneumoniae* are conserved across all chlamydiae, but 98kDa, 76 kDa and 54 kDa proteins appear to be *C. pneumoniae*-specific (Campos *et al.* (1995) Investigation of Ophthalmology and Visual Science 36:1477; Marrie (1993) Clinical Infectious Diseases. 18:501; Wiedmann-Al-Ahmad M, *et al.* Reactions of polyclonal and neutralizing anti-p54 monoclonal antibodies with an isolated,

species-specific 54-kilodalton protein of Chlamydia pneumoniae. Clin Diagn Lab Immunol. 1997 Nov; 4(6): 700-704). A publication relevant to 98 KDa proteins is Perez Melgosa et al. FEMS Microbiology Letters. 112(2): 199-204. 1993. Another relevant publication is Knudsen, Database EMBL, accession number 086164, 01-11-1998.

Immunoblotting of isolates with sera from patients does show variation of blotting patterns between isolates, indicating that serotypes *C. pneumoniae* may exist (Grayston et al. (1995) Journal of Infectious Diseases 168:1231; Ramirez et al (1996) Annals of Internal Medicine 125:979). However, the results are potentially confouned by the infection status of the patients, since immunoblot profiles of a patient's sera change with time post-infection. An assessment of the number and relative frequency of any serotypes, and the defining antigens, is not yet possible.

Accordingly, a need exists for identifying and isolating polynucleotide sequences of *C. pneumoniae* for use in preventing and treating Chlamydia infection.

SUMMARY OF THE INVENTION

The present invention provides purified and isolated polynucleotide molecules that encode *Chlamydia* polypeptides which can be used in methods to prevent, treat, and diagnose *Chlamydia* infection. In one form of the invention, the polynucleotide molecules are selected from DNA that encode polypeptides CPN100634 (SEQ ID. Nos: 1 and 2), CPN100635 (SEQ ID Nos: 3 and 4), CPN100638 (SEQ ID Nos: 5 and 6), CPN100639 (SEQ ID Nos: 7 and 8), and CPN100708 (SEQ ID Nos: 9 and 10).

Another form of the invention provides polypeptides corresponding to the isolated DNA molecules. The amino acid sequences of the corresponding encoded polypeptides are shown for CPN100634 as SEQ ID No: 11, CPN100635 as SEQ ID Nos: 12 and 13, CPN100638 as SEQ ID No: 14, CPN100639 as SEQ ID No: 15, and CPN 100708 as SEQ ID No: 16.

Those skilled in the art will readily understand that the invention, having provided the polynucleotide sequences encoding *Chlamydia* polypeptides, also provides polynucleotides encoding

fragments derived from such peptides. Moreover, the invention is understood to provide mutants and derivatives of such polypeptides and fragments derived therefrom, which result from the addition, deletion, or substitution of non-essential amino acids as described herein. Those skilled in the art would also readily understand that the invention, having provided the polynucleotide sequences encoding Chlamydia polypeptides, further provides monospecific antibodies that specifically bind to such polypeptides.

The present invention has wide application and includes expression cassettes, vectors, and cells transformed or transfected with the polynucleotides of the invention. Accordingly, the present invention further provides (i) a method for producing a polypeptide of the invention in a recombinant host system and related expression cassettes, vectors, and transformed or transfected cells; (ii) a vaccine, or a live vaccine vector such as a pox virus, *Salmonella typhimurium*, or *Vibrio cholerae* vector, containing a polynucleotide of the invention, such vaccines and vaccine vectors being useful for, *e.g.*, preventing and treating *Chlamydia* infection, in combination with a diluent or carrier, and related pharmaceutical compositions and associated therapeutic and/or prophylactic methods; (iii) a therapeutic and/or prophylactic use of an RNA or DNA molecule of the invention, either in a naked form or formulated with a delivery vehicle, a polypeptide or combination of polypeptides, or a monospecific antibody of the invention, and related pharmaceutical compositions; (iv) a method for diagnosing the presence of *Chlamydia* in a biological sample, which can involve the use of a DNA or RNA molecule, a monospecific antibody, or a polypeptide of the invention; and (v) a method for purifying a polypeptide of the invention by antibody-based affinity chromatography.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will be further understood from the following description with reference to the drawings, in which:

Figure 1 shows the nucleotide sequence of the CPN100634 (SEQ ID No: 1 - entire sequence and SEQ ID No: 2 - coding sequence) and the deduced amino acid sequence of the CPN100634 protein from *Chlamydia pneumoniae* (SEQ ID No: 11).

Figure 2 shows the restriction enzyme analysis of the gene encoding the *C. pneumoniae* CPN100634 gene.

Figure 3 shows the nucleotide sequence of the CPN100635 (SEQ ID No: 3 - entire sequence and SEQ ID No: 4 - coding sequence) and the deduced amino acid sequence of the CPN100635 protein from *Chlamydia pneumoniae* (SEQ ID No: 12 - entire amino acid sequence corresponding to the open reading frame, and 13 - the post-translationally processed polypeptide).

Figure 4 shows the restriction enzyme analysis of the gene encoding the *C. pneumoniae* CPN100635 gene.

Figure 5 shows the nucleotide sequence of the CPN100638 (SEQ ID No: 5 - entire sequence and SEQ ID No: 6 - coding sequence) and the deduced amino acid sequence of the CPN100638 protein from *Chlamydia pneumoniae* (SEQ ID No: 14). The sequence is encoded on the negative strand.

Figure 6 shows the restriction enzyme analysis of the gene encoding the *C. pneumoniae* CPN100638 gene.

Figure 7 shows the nucleotide sequence of the CPN100639 (SEQ ID No: 7 - entire sequence and SEQ ID No: 8 - coding sequence) and the deduced amino acid sequence of the CPN100639 protein from *Chlamydia pneumoniae* (SEQ ID No: 15).

Figure 8 shows the restriction enzyme analysis of the gene encoding the *C. pneumoniae* CPN100639 gene.

Figure 9 shows the nucleotide sequence of the CPN100708 (SEQ ID No: 9 - entire sequence and SEQ ID No: 10 - coding sequence coded for on the negative strand) and the deduced amino

acid sequence of the CPN100708 protein from *Chlamydia pneumoniae* (SEQ ID No: 16).

Figure 10 shows the restriction enzyme analysis of the gene encoding the *C. pneumoniae* CPN100708 gene.

Figures 11 through 15 show an identification of T and B cell epitopes from the amino acid sequences shown in the foregoing figures.

DETAILED DESCRIPTION OF INVENTION

Open reading frames (ORFs) encoding chlamydial polypeptides have been identified from the *C. pneumoniae* genome. These polypeptides include polypeptides found permanently in the bacterial membrane structure, polypeptides present in the external vicinity of the bacterial membrane, polypeptides found permanently in the inclusion membrane structure, polypeptides present in the external vicinity of the inclusion membrane, and polypeptides released into the cytoplasm of the infected cell. These polypeptides can be used to prevent and treat *Chlamydia* infection.

According to a first aspect of the invention, isolated polynucleotides are provided which encode the precursor and mature forms of *Chlamydia* polypeptides, whose amino acid sequences are selected from the group consisting of: SEQ ID Nos: 11 to 16.

The term "isolated polynucleotide" is defined as a polynucleotide removed from the environment in which it naturally occurs. For example, a naturally-occurring DNA molecule present in the genome of a living bacteria or as part of a gene bank is not isolated, but the same molecule separated from the remaining part of the bacterial genome, as a result of, e.g., a cloning event (amplification), is isolated. Typically, an isolated DNA molecule is free from DNA regions (e.g., coding regions) with which it is immediately contiguous at the 5' or 3' end, in the naturally occurring genome. Such isolated

polynucleotides may be part of a vector or a composition and still be defined as isolated in that such a vector or composition is not part of the natural environment of such polynucleotide.

The polynucleotide of the invention is either RNA or DNA (cDNA, genomic DNA, or synthetic DNA), or modifications, variants, homologs or fragments thereof. The DNA is either double-stranded or single-stranded, and, if single-stranded, is either the coding strand or the non-coding (anti-sense) strand. Any one of the sequences that encode the polypeptides of the invention as shown in SEQ ID Nos: 1 to 10 is (a) a coding sequence, (b) a ribonucleotide sequence derived from transcription of (a), or (c) a coding sequence which uses the redundancy or degeneracy of the genetic code to encode the same polypeptides. By "polypeptide" or "protein" is meant any chain of amino acids, regardless of length or post-translational modification (*e.g.*, glycosylation or phosphorylation). Both terms are used interchangeably in the present application.

Consistent with the first aspect of the invention, amino acid sequences are provided which are homologous to any one of SEQ ID Nos: 11 to 16. As used herein, "homologous amino acid sequence" is any polypeptide which is encoded, in whole or in part, by a nucleic acid sequence which hybridizes at 25-35°C below critical melting temperature (Tm), to any portion of the nucleic acid sequences of SEQ ID Nos: 1 to 10. A homologous amino acid sequence is one that differs from an amino acid sequence shown in any one of SEQ ID Nos: 11 to 16 by one or more conservative amino acid substitutions. Such a sequence also encompass serotypic variants (defined below) as well as sequences containing deletions or insertions which retain inherent characteristics of the polypeptide such as immunogenicity. Preferably, such a sequence is at least 75%, more preferably 80%, and most preferably 90% identical to any one of SEQ ID Nos: 11 to 16.

Homologous amino acid sequences include sequences that are identical or substantially identical to SEQ ID Nos: 11 to 16. By "amino acid sequence substantially identical" is meant a sequence that is at least 90%, preferably 95%, more preferably 97%, and most preferably 99% identical to an amino acid sequence of reference and that preferably differs from the sequence of reference by a majority of conservative amino acid substitutions.

Conservative amino acid substitutions are substitutions among amino acids of the same class. These classes include, for example, amino acids having uncharged polar side chains, such as asparagine, glutamine, serine, threonine, and tyrosine; amino acids having basic side chains, such as lysine, arginine, and histidine; amino acids having acidic side chains, such as aspartic acid and glutamic acid; and amino acids having nonpolar side chains, such as glycine, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan, and cysteine.

Homology is measured using sequence analysis software such as Sequence Analysis Software Package of the Genetics Computer Group, University of Wisconsin Biotechnology Center, 1710 University Avenue, Madison, WI 53705. Amino acid sequences are aligned to maximize identity. Gaps may be artificially introduced into the sequence to attain proper alignment. Once the optimal alignment has been set up, the degree of homology is established by recording all of the positions in which the amino acids of both sequences are identical, relative to the total number of positions.

Homologous polynucleotide sequences are defined in a similar way. Preferably, a homologous sequence is one that is at least 45%, more preferably 60%, and most preferably 85% identical to any one of coding sequences SEQ ID Nos: 1 to 10.

Consistent with the first aspect of the invention, polypeptides having a sequence homologous to any one of SEQ ID

Nos: 11 to 16 include naturally-occurring allelic variants, as well as mutants or any other non-naturally occurring variants that retain the inherent characteristics of the polypeptide of SEQ ID Nos: 11 to 16.

As is known in the art, an allelic variant is an alternate form of a polypeptide that is characterized as having a substitution, deletion, or addition of one or more amino acids that does not alter the biological function of the polypeptide. By "biological function" is meant the function of the polypeptide in the cells in which it naturally occurs, even if the function is not necessary for the growth or survival of the cells. For example, the biological function of a porin is to allow the entry into cells of compounds present in the extracellular medium. Biological function is distinct from antigenic property. A polypeptide can have more than one biological function.

Allelic variants are very common in nature. For example, a bacterial species such as *C. pneumoniae*, is usually represented by a variety of strains that differ from each other by minor allelic variations. Indeed, a polypeptide that fulfills the same biological function in different strains can have an amino acid sequence (and polynucleotide sequence) that is not identical in each of the strains. Despite this variation, an immune response directed generally against many allelic variants has been demonstrated. In studies of the *Chlamydial* MOMP antigen, cross-strain antibody binding plus neutralization of infectivity occurs despite amino acid sequence variation of MOMP from strain to strain, indicating that the MOMP, when used as an immunogen, is tolerant of amino acid variations.

Polynucleotides encoding homologous polypeptides or allelic variants are retrieved by polymerase chain reaction (PCR) amplification of genomic bacterial DNA extracted by conventional methods. This involves the use of synthetic

oligonucleotide primers matching upstream and downstream of the 5' and 3' ends of the encoding domain. Suitable primers are designed according to the nucleotide sequence information provided in SEQ ID Nos: 1 to 10. The procedure is as follows: a primer is selected which consists of 10 to 40, preferably 15 to 25 nucleotides. It is advantageous to select primers containing C and G nucleotides in a proportion sufficient to ensure efficient hybridization; *i.e.*, an amount of C and G nucleotides of at least 40%, preferably 50% of the total nucleotide content.A standard PCR reaction contains typically 0.5 to 5 Units of Taq DNA polymerase per 100 µL, 20 to 200 µM deoxynucleotide each, preferably at equivalent concentrations, 0.5 to 2.5 MM magnesium over the total deoxynucleotide concentration, 10^5 to 10^6 target molecules, and about 20 pmol of each primer. About 25 to 50 PCR cycles are performed, with an annealing temperature 15°C to 5°C below the true Tm of the primers. A more stringent annealing temperature improves discrimination against incorrectly annealed primers and reduces incorportion of incorrect nucleotides at the 3' end of primers. A denaturation temperature of 95°C to 97°C is typical, although higher temperatures may be appropriate for dematuration of G+C-rich targets. The number of cycles performed depends on the starting concentration of target molecules, though typically more than 40 cycles is not recommended as non-specific background products tend to accumulate.

An alternative method for retrieving polynucleotides encoding homologous polypeptides or allelic variants is by hybridization screening of a DNA or RNA library. Hybridization procedures are well-known in the art and are described in Ausubel *et al.*, (Ausubel *et al.*, Current Protocols in Molecular Biology, John Wiley & Sons Inc., 1994), Silhavy *et al.* (Silhavy *et al.* Experiments with Gene Fusions, Cold Spring Harbor Laboratory Press, 1984), and Davis *et al.* (Davis *et al.* A Manual

for Genetic Engineering: Advanced Bacterial Genetics, Cold Spring Harbor Laboratory Press, 1980)). Important parameters for optimizing hybridization conditions are reflected in a formula used to obtain the critical melting temperature above which two complementary DNA strands separate from each other (Casey & Davidson, Nucl. Acid Res. (1977) 4:1539). For polynucleotides of about 600 nucleotides or larger, this formula is as follows: Tm = 81.5 + 0.5 x (% G+C) + 1.6 log (positive ion concentration) - 0.6 x (% formamide). Under appropriate stringency conditions, hybridization temperature (Th) is approximately 20 to 40°C, 20 to 25°C, or, preferably 30 to 40°C below the calculated Tm. Those skilled in the art will understand that optimal temperature and salt conditions can be readily determined.

For the polynucleotides of the invention, stringent conditions are achieved for both pre-hybridizing and hybridizing incubations (i) within 4-16 hours at 42°C, in 6 x SSC containing 50% formamide, or (ii) within 4-16 hours at 65°C in an aqueous 6 x SSC solution (1 M NaCl, 0.1 M sodium citrate (pH 7.0)).

Useful homologs and fragments thereof that do not occur naturally are designed using known methods for identifying regions of an antigen that are likely to tolerate amino acid sequence changes and/or deletions. As an example, homologous polypeptides from different species are compared; conserved sequences are identified. The more divergent sequences are the most likely to tolerate sequence changes. Homology among sequences may be analyzed using the BLAST homology searching algorithm of Altschul et al., Nucleic Acids Res.25:3389-3402 (1997). Alternatively, sequences are modified such that they become more reactive to T- and/or B-cells. (See Figures 11 to 15 below for identification of T- and B- epitopes). Yet another alternative is to mutate a particular amino acid residue or sequence within the polypeptide *in vitro*, then screen the mutant

polypeptides for their ability to prevent or treat Chlamydia infection according to the method outlined below.

A person skilled in the art will readily understand that by following the screening process of this invention, it will be determined without undue experimentation whether a particular homolog of any of SEQ ID Nos: 11 to 16 may be useful in the prevention or treatment of Chlamydia infection. The screening procedure comprises the steps:

(i) immunizing an animal, preferably mouse, with the test homolog or fragment;

(ii) inoculating the immunized animal with Chlamydia; and,

(iii) selecting those homologs or fragments which confer protection against Chlamydia.

By "conferring protection" is meant that there is a reduction is severity of any of the effects of Chlamydia infection, in comparison with a control animal which was not immunized with the test homolog or fragment.

It has been previously demonstrated (Yang, Z. P., Chi, E. Y., Kuo, C. C. and Grayston, J. T. 1993. A mouse model of *C. pneumoniae* strain TWAR pneumonitis. 61(5):2037-2040) that mice are susceptible to intranasal infection with different isolates of *C. pneumoniae*. Strain AR-39 (Chi, E. Y., Kuo, C. C. and Grayston, J. T. , 1987. Unique ultrastructure in the elementary body of Chlamydia sp. strain TWAR. J. Bacteriol. 169(8):3757-63) was used in Balb/c mice as a challenge infection model to examine the capacity of chlamydia gene products delivered as naked DNA to elicit a protective response against a sublethal *C. pneumoniae* lung infection. Protective immunity is defined as an accelerated clearance of pulmonary infection.

Groups of 7 to 9 week old male Balb/c mice (6 to 10 per group) were immunized intramuscularly (i.m.) plus intranasally (i.n.) with plasmid DNA containing the coding sequence of a *C. pneumoniae* polypeptide. Saline or the plasmid vector lacking

an inserted chlamydial gene was given to groups of control animals.

For i.m. immunization alternate left and right quadriceps were injected with 100µg of DNA in 50µl of PBS on three occasions at 0, 3 and 6 weeks. For i.n. immunization, anaesthetized mice aspirated 50µl of PBS containing 50 µg DNA on three occasions at 0, 3 and 6 weeks. At week 8, immunized mice were inoculated i.n. with 5 x 10^5 IFU of *C. pneumoniae*, strain AR39 in 100µl of SPG buffer to test their ability to limit the growth of a sublethal *C. pneumoniae* challenge.

Lungs were taken from mice at day 9 post-challenge and immediately homogenised in SPG buffer (7.5% sucrose, 5mM glutamate, 12.5mM phosphate pH7.5). The homogenate was stored frozen at -70°C until assay. Dilutions of the homogenate were assayed for the presence of infectious chlamydia by inoculation onto monolayers of susceptible cells. The inoculum was centrifuged onto the cells at 3000rpm for 1 hour, then the cells were incubated for three days at 35°C in the presence of 1µg/ml cycloheximide. After incubation the monolayers were fixed with formalin and methanol then immunoperoxidase stained for the presence of chlamydial inclusions using convalescent sera from rabbits infected with *C. pneumoniae* and metal-enhanced DAB as a peroxidase substrate.

Consistent with the first aspect of the invention, polypeptide derivatives are provided that are partial sequences of SEQ ID Nos: 11 to 16, partial sequences of polypeptide sequences homologous to SEQ ID Nos: 11 to 16, polypeptides derived from full-length polypeptides by internal deletion, and fusion proteins.

It is an accepted practice in the field of immunology to use fragments and variants of protein immunogens as vaccines, as all that is required to induce an immune response to a protein is a small (*e.g.*, 8 to 10 amino acid) immunogenic region of the

protein. Various short synthetic peptides corresponding to surface-exposed antigens of pathogens other than *Chlamydia* have been shown to be effective vaccine antigens against their respective pathogens, *e.g.* an 11 residue peptide of murine mammary tumor virus (Casey & Davidson, Nucl. Acid Res. (1977) 4:1539), a 16-residue peptide of Semliki Forest virus (Snijders *et al.*, 1991. J. Gen. Virol. 72:557-565), and two overlapping peptides of 15 residues each from canine parvovirus (Langeveld *et al.*, Vaccine 12(15):1473-1480, 1994).

Accordingly, it will be readily apparent to one skilled in the art, having read the present description, that partial sequences of SEQ ID Nos: 11 to 16 or their homologous amino acid sequences are inherent to the full-length sequences and are taught by the present invention. Such polypeptide fragments preferably are at least 12 amino acids in length. Advantageously, they are at least 20 amino acids, preferably at least 50 amino acids, more preferably at least 75 amino acids, and most preferably at least 100 amino acids in length.

Polynucleotides of 30 to 600 nucleotides encoding partial sequences of sequences homologous to SEQ ID Nos: 11 to 16 are retrieved by PCR amplification using the parameters outlined above and using primers matching the sequences upstream and downstream of the 5' and 3' ends of the fragment to be amplified. The template polynucleotide for such amplification is either the full length polynucleotide homologous to one of SEQ ID Nos: 1 to 10, or a polynucleotide contained in a mixture of polynucleotides such as a DNA or RNA library. As an alternative method for retrieving the partial sequences, screening hybridization is carried out under conditions described above and using the formula for calculating Tm. Where fragments of 30 to 600 nucleotides are to be retrieved, the calculated Tm is corrected by subtracting (600/polynucleotide size in base pairs) and the stringency conditions are defined by a hybridization temperature that is 5 to 10°C below Tm. Where

oligonucleotides shorter than 20-30 bases are to be obtained, the formula for calculating the Tm is as follows: Tm = 4 x (G+C) + 2 (A+T). For example, an 18 nucleotide fragment of 50% G+C would have an approximate Tm of 54°C. Short peptides that are fragments of SEQ. ID Nos. 11 to 16 or their homologous sequences, are obtained directly by chemical synthesis (E. Gross and H. J. Meinhofer, 4 The Peptides: Analysis, Synthesis, Biology; Modern Techniques of Peptide Synthesis, John Wiley & Sons (1981), and M. Bodanzki, Principles of Peptide Synthesis, Springer -Verlag (1984)).

Useful polypeptide derivatives, *e.g.*, polypeptide fragments, are designed using computer-assisted analysis of amino acid sequences. This identifies probable surface-exposed, antigenic regions (Hughes *et al.*, 1992. Infect. Immun. 60(9):3497). An analysis of the 6 amino acid sequences contained in SEQ ID Nos: 11 to 16, based on the product of flexibility and hydrophobicity propensities using the program SEQSEE (Wishart DS, et al. "SEQSEE: a comprehensive program suite for protein sequence analysis." *Comput Appl Biosci*. 1994 Apr;10(2):121-32), reveal a number of potential B- and T-cell epitopes which may be used as a basis for selecting useful immunogenic fragments and variants. The results are shown in Figures 11 to 15. This analysis uses a reasonable combination of external surface features that is likely to be recognized by antibodies. Probable T-cell epitopes for HLA-A0201 MHC subclass were revealed by an algorithm written at Connaught Laboratories that emulates an approach developed at the NIH (Parker KC, *et al.* "Peptide binding to MHC class I molecules: implications for antigenic peptide prediction." *Immunol Res* 1995;14(1):34-57).

Epitopes which induce a protective T cell-dependent immune response are present throughout the length of the polypeptide. However, some epitopes may be masked by secondary and tertiary structures of the polypeptide. To reveal such masked epitopes large internal deletions are created which

remove much of the original protein structure and exposes the masked epitopes. Such internal deletions sometimes effects the additional advantage of removing immunodominant regions of high variability among strains. Polynucleotides encoding polypeptide fragments and polypeptides having large internal deletions are constructed using standard methods (Ausubel *et al.*, Current Protocols in Molecular Biology, John Wiley & Sons Inc., 1994). Such methods include standard PCR, inverse PCR, restriction enzyme treatment of cloned DNA molecules, or the method of Kunkel *et al.* (Kunkel *et al.* Proc. Natl. Acad. Sci. USA (1985) 82:448). Components for these methods and instructions for their use are readily available from various commercial sources such as Stratagene. Once the deletion mutants have been constructed, they are tested for their ability to prevent or treat Chlamydia infection as described above.

As used herein, a fusion polypeptide is one that contains a polypeptide or a polypeptide derivative of the invention fused at the N- or C-terminal end to any other polypeptide (hereinafter referred to as a peptide tail). A simple way to obtain such a fusion polypeptide is by translation of an in-frame fusion of the polynucleotide sequences, *i.e.*, a hybrid gene. The hybrid gene encoding the fusion polypeptide is inserted into an expression vector which is used to transform or transfect a host cell. Alternatively, the polynucleotide sequence encoding the polypeptide or polypeptide derivative is inserted into an expression vector in which the polynucleotide encoding the peptide tail is already present. Such vectors and instructions for their use are commercially available, *e.g.* the pMal-c2 or pMal-p2 system from New England Biolabs, in which the peptide tail is a maltose binding protein, the glutathione-S-transferase system of Pharmacia, or the His-Tag system available from Novagen. These and other expression systems provide convenient means for further purification of polypeptides and derivatives of the invention.

An advantageous example of a fusion polypeptide is one where the polypeptide or homolog or fragment of the invention is fused to a polypeptide having adjuvant activity, such as subunit B of either cholera toxin or *E. coli* heat-labile toxin. Another advantageous fusion is one where the polypeptide, homolog or fragment is fused to a strong T-cell epitope or B-cell epitope. Such an epitope may be one known in the art (*e.g.* the Hepatitis B virus core antigen, D.R. Millich et al., "Antibody production to the nucleocapsid and envelope of the Hepatitis B virus primed by a single synthetic T cell site", Nature. 1987. 329:547-549), or one which has been identified in another polypeptide of the invention (Figures 11-15). Consistent with this aspect of the invention is a fusion polypeptide comprising T- or B-cell epitopes from one of SEQ ID Nos: 11 to 16 or its homolog or fragment, wherein the epitopes are derived from multiple variants of said polypeptide or homolog or fragment, each variant differing from another in the location and sequence of its epitope within the polypeptide. Such a fusion is effective in the prevention and treatment of Chlamydia infection since it optimizes the T- and B-cell response to the overall polypeptide, homolog or fragment.

To effect fusion, the polypeptide of the invention is fused to the N-, or preferably, to the C-terminal end of the polypeptide having adjuvant activity or T- or B-cell epitope. Alternatively, a polypeptide fragment of the invention is inserted internally within the amino acid sequence of the polypeptide having adjuvant activity. The T- or B-cell epitope may also be inserted internally within the amino acid sequence of the polypeptide of the invention.

Consistent with the first aspect, the polynucleotides of the invention also encode hybrid precursor polypeptides containing heterologous signal peptides, which mature into polypeptides of the invention. By "heterologous signal peptide"

is meant a signal peptide that is not found in naturally-occurring precursors of polypeptides of the invention.

A polynucleotide molecule according to the invention, including RNA, DNA, or modifications or combinations thereof, have various applications. A DNA molecule is used, for example, (i) in a process for producing the encoded polypeptide in a recombinant host system, (ii) in the construction of vaccine vectors such as poxviruses, which are further used in methods and compositions for preventing and/or treating *Chlamydia* infection, (iii) as a vaccine agent (as well as an RNA molecule), in a naked form or formulated with a delivery vehicle and, (iv) in the construction of attenuated *Chlamydia* strains that can over-express a polynucleotide of the invention or express it in a non-toxic, mutated form.

Accordingly, a second aspect of the invention encompasses (i) an expression cassette containing a DNA molecule of the invention placed under the control of the elements required for expression, in particular under the control of an appropriate promoter; (ii) an expression vector containing an expression cassette of the invention; (iii) a procaryotic or eucaryotic cell transformed or transfected with an expression cassette and/or vector of the invention, as well as (iv) a process for producing a polypeptide or polypeptide derivative encoded by a polynucleotide of the invention, which involves culturing a procaryotic or eucaryotic cell transformed or transfected with an expression cassette and/or vector of the invention, under conditions that allow expression of the DNA molecule of the invention and, recovering the encoded polypeptide or polypeptide derivative from the cell culture.

A recombinant expression system is selected from procaryotic and eucaryotic hosts. Eucaryotic hosts include yeast cells (*e.g.*, *Saccharomyces cerevisiae* or *Pichia pastoris*), mammalian cells (*e.g.*, COS1, NIH3T3, or JEG3 cells), arthropods cells (*e.g.*, *Spodoptera frugiperda* (SF9) cells), and plant

cells. A preferred expression system is a procaryotic host such as *E. coli*. Bacterial and eucaryotic cells are available from a number of different sources including commercial sources to those skilled in the art, e.g., the American Type Culture Collection (ATCC; Rockville, Maryland). Commercial sources of cells used for recombinant protein expression also provide instructions for usage of the cells.

The choice of the expression system depends on the features desired for the expressed polypeptide. For example, it may be useful to produce a polypeptide of the invention in a particular lipidated form or any other form.

One skilled in the art would readily understand that not all vectors and expression control sequences and hosts would be expected to express equally well the polynucleotides of this invention. With the guidelines described below, however, a selection of vectors, expression control sequences and hosts may be made without undue experimentation and without departing from the scope of this invention.

In selecting a vector, the host must be chosen that is compatible with the vector which is to exist and possibly replicate in it. Considerations are made with respect to the vector copy number, the ability to control the copy number, expression of other proteins such as antibiotic resistance. In selecting an expression control sequence, a number of variables are considered. Among the important variable are the relative strength of the sequence (e.g. the ability to drive expression under various conditions), the ability to control the sequence's function, compatibility between the polynucleotide to be expressed and the control sequence (e.g. secondary structures are considered to avoid hairpin structures which prevent efficient transcription). In selecting the host, unicellular hosts are selected which are compatible with the selected vector, tolerant of any possible toxic effects of the expressed product, able to secrete the expressed product efficiently if

such is desired, to be able to express the product in the desired conformation, to be easily scaled up, and to which ease of purification of the final product.

The choice of the expression cassette depends on the host system selected as well as the features desired for the expressed polypeptide. Typically, an expression cassette includes a promoter that is functional in the selected host system and can be constitutive or inducible; a ribosome binding site; a start codon (ATG) if necessary; a region encoding a signal peptide, *e.g.*, a lipidation signal peptide; a DNA molecule of the invention; a stop codon; and optionally a 3' terminal region (translation and/or transcription terminator). The signal peptide encoding region is adjacent to the polynucleotide of the invention and placed in proper reading frame. The signal peptide-encoding region is homologous or heterologous to the DNA molecule encoding the mature polypeptide and is compatible with the secretion apparatus of the host used for expression. The open reading frame constituted by the DNA molecule of the invention, solely or together with the signal peptide, is placed under the control of the promoter so that transcription and translation occur in the host system. Promoters and signal peptide encoding regions are widely known and available to those skilled in the art and include, for example, the promoter of *Salmonella typhimurium* (and derivatives) that is inducible by arabinose (promoter araB) and is functional in Gram-negative bacteria such as *E. coli* (as described in U.S. Patent No. 5,028,530 and in Cagnon *et al.*, (Cagnon *et al.*, Protein Engineering (1991) 4(7):843)); the promoter of the gene of bacteriophage T7 encoding RNA polymerase, that is functional in a number of *E. coli* strains expressing T7 polymerase (described in U.S. Patent No. 4,952,496); OspA lipidation signal peptide ; and RlpB lipidation signal peptide (Takase *et al.*, J. Bact. (1987) 169:5692).

The expression cassette is typically part of an expression vector, which is selected for its ability to replicate in the chosen expression system. Expression vectors (*e.g.*, plasmids or viral vectors) can be chosen, for example, from those described in Pouwels *et al.* (Cloning Vectors: A Laboratory Manual 1985, Supp. 1987). Suitable expression vectors can be purchased from various commercial sources.

Methods for transforming/transfecting host cells with expression vectors are well-known in the art and depend on the host system selected as described in Ausubel *et al.*, (Ausubel *et al.*, Current Protocols in Molecular Biology, John Wiley & Sons Inc., 1994).

Upon expression, a recombinant polypeptide of the invention (or a polypeptide derivative) is produced and remains in the intracellular compartment, is secreted/excreted in the extracellular medium or in the periplasmic space, or is embedded in the cellular membrane. The polypeptide is recovered in a substantially purified form from the cell extract or from the supernatant after centrifugation of the recombinant cell culture. Typically, the recombinant polypeptide is purified by antibody-based affinity purification or by other well-known methods that can be readily adapted by a person skilled in the art, such as fusion of the polynucleotide encoding the polypeptide or its derivative to a small affinity binding domain. Antibodies useful for purifying by immunoaffinity the polypeptides of the invention are obtained as described below.

A polynucleotide of the invention can also be useful as a vaccine. There are two major routes, either using a viral or bacterial host as gene delivery vehicle (live vaccine vector) or administering the gene in a free form, *e.g.*, inserted into a plasmid. Therapeutic or prophylactic efficacy of a polynucleotide of the invention is evaluated as described below.

Accordingly, a third aspect of the invention provides (i) a vaccine vector such as a poxvirus, containing a DNA molecule

of the invention, placed under the control of elements required for expression; (ii) a composition of matter comprising a vaccine vector of the invention, together with a diluent or carrier; specifically (iii) a pharmaceutical composition containing a therapeutically or prophylactically effective amount of a vaccine vector of the invention; (iv) a method for inducing an immune response against *Chlamydia* in a mammal (*e.g.*, a human; alternatively, the method can be used in veterinary applications for treating or preventing *Chlamydia* infection of animals, *e.g.*, cats or birds), which involves administering to the mammal an immunogenically effective amount of a vaccine vector of the invention to elicit a protective or therapeutic immune response to *Chlamydia* ; and particularly, (v) a method for preventing and/or treating a *Chlamydia* (*e.g.*, *C. trachomatis, C. psittaci, C. pneumonia, C. pecorum*) infection, which involves administering a prophylactic or therapeutic amount of a vaccine vector of the invention to an infected individual. Additionally, the third aspect of the invention encompasses the use of a vaccine vector of the invention in the preparation of a medicament for preventing and/or treating *Chlamydia* infection.

As used herein, a vaccine vector expresses one or several polypeptides or derivatives of the invention. The vaccine vector may express additionally a cytokine, such as interleukin-2 (IL-2) or interleukin-12 (IL-12), that enhances the immune response (adjuvant effect). It is understood that each of the components to be expressed is placed under the control of elements required for expression in a mammalian cell.

Consistent with the third aspect of the invention is a composition comprising several vaccine vectors, each of them capable of expressing a polypeptide or derivative of the invention. A composition may also comprise a vaccine vector capable of expressing an additional *Chlamydia* antigen, or a

subunit, fragment, homolog, mutant, or derivative thereof, optionally together with a cytokine such as IL-2 or IL-12.

Vaccination methods for treating or preventing infection in a mammal comprises use of a vaccine vector of the invention to be administered by any conventional route, particularly to a mucosal (*e.g.*, ocular, intranasal, oral, gastric, pulmonary, intestinal, rectal, vaginal, or urinary tract) surface or *via* the parenteral (*e.g.*, subcutaneous, intradermal, intramuscular, intravenous, or intraperitoneal) route. Preferred routes depend upon the choice of the vaccine vector. Treatment may be effected in a single dose or repeated at intervals. The appropriate dosage depends on various parameters understood by skilled artisans such as the vaccine vector itself, the route of administration or the condition of the mammal to be vaccinated (weight, age and the like).

Live vaccine vectors available in the art include viral vectors such as adenoviruses and poxviruses as well as bacterial vectors, *e.g.*, *Shigella*, *Salmonella*, *Vibrio cholerae*, *Lactobacillus*, Bacille bilié de Calmette-Guérin (BCG), and *Streptococcus*.

An example of an adenovirus vector, as well as a method for constructing an adenovirus vector capable of expressing a DNA molecule of the invention, are described in U.S. Patent No. 4,920,209. Poxvirus vectors include vaccinia and canary pox virus, described in U.S. Patent No. 4,722,848 and U.S. Patent No. 5,364,773, respectively. (Also see, *e.g.*, Tartaglia *et al.*, Virology (1992) 188:217) for a description of a vaccinia virus vector and Taylor *et al*, Vaccine (1995) 13:539 for a reference of a canary pox.) Poxvirus vectors capable of expressing a polynucleotide of the invention are obtained by homologous recombination as described in Kieny *et al.*, Nature (1984) 312:163 so that the polynucleotide of the invention is inserted in the viral genome under appropriate conditions for expression in mammalian cells. Generally, the dose of vaccine viral

vector, for therapeutic or prophylactic use, can be of from about $1x10^4$ to about $1x10^{11}$, advantageously from about $1x10^7$ to about $1x10^{10}$, preferably of from about $1x10^7$ to about $1x10^9$ plaque-forming units per kilogram. Preferably, viral vectors are administered parenterally; for example, in 3 doses, 4 weeks apart. It is preferable to avoid adding a chemical adjuvant to a composition containing a viral vector of the invention and thereby minimizing the immune response to the viral vector itself.

Non-toxicogenic *Vibrio cholerae* mutant strains that are useful as a live oral vaccine are known. Mekalanos *et al.*, Nature (1983) 306:551 and U.S. Patent No. 4,882,278 describe strains which have a substantial amount of the coding sequence of each of the two *ctxA* alleles deleted so that no functional *cholerae* toxin is produced. WO 92/11354 describes a strain in which the *irgA* locus is inactivated by mutation; this mutation can be combined in a single strain with *ctxA* mutations. WO 94/01533 describes a deletion mutant lacking functional *ctxA* and *attRS1* DNA sequences. These mutant strains are genetically engineered to express heterologous antigens, as described in WO 94/19482. An effective vaccine dose of a *Vibrio cholerae* strain capable of expressing a polypeptide or polypeptide derivative encoded by a DNA molecule of the invention contains about $1x10^5$ to about $1x10^9$, preferably about $1x10^6$ to about $1x10^8$, viable bacteria in a volume appropriate for the selected route of administration. Preferred routes of administration include all mucosal routes; most preferably, these vectors are administered intranasally or orally.

Attenuated *Salmonella typhimurium* strains, genetically engineered for recombinant expression of heterologous antigens or not, and their use as oral vaccines are described in Nakayama *et al.* (Bio/Technology (1988) 6:693) and WO 92/11361. Preferred routes of administration include all mucosal routes;

most preferably, these vectors are administered intranasally or orally.

Other bacterial strains used as vaccine vectors in the context of the present invention are described for *Shigella flexneri* in High *et al.*, EMBO (1992) 11:1991 and Sizemore *et al.*, Science (1995) 270:299; for *Streptococcus gordonii* in Medaglini *et al.*, Proc. Natl. Acad. Sci. USA (1995) 92:6868; and for Bacille Calmette Guerin in Flynn J.L., Cell. Mol. Biol. (1994) 40 (suppl. I):31, WO 88/06626, WO 90/00594, WO 91/13157, WO 92/01796, and WO 92/21376.

In bacterial vectors, the polynucleotide of the invention is inserted into the bacterial genome or remains in a free state as part of a plasmid.

The composition comprising a vaccine bacterial vector of the present invention may further contain an adjuvant . A number of adjuvants are known to those skilled in the art. Preferred adjuvants as provided below.

Accordingly, a fourth aspect of the invention provides (i) a composition of matter comprising a polynucleotide of the invention, together with a diluent or carrier; (ii) a pharmaceutical composition comprising a therapeutically or prophylactically effective amount of a polynucleotide of the invention; (iii) a method for inducing an immune response against *Chlamydia* in a mammal by administration of an immunogenically effective amount of a polynucleotide of the invention to elicit a protective immune response to *Chlamydia*; and particularly, (iv) a method for preventing and/or treating a *Chlamydia* (*e.g., C. trachomatis, C. psittaci, C. pneumoniae, or C. pecorum*) infection, by administering a prophylactic or therapeutic amount of a polynucleotide of the invention to an infected individual. Additionally, the fourth aspect of the invention encompasses the use of a polynucleotide of the invention in the preparation of a medicament for preventing and/or treating *Chlamydia* infection. A preferred use includes

the use of a DNA molecule placed under conditions for expression in a mammalian cell, especially in a plasmid that is unable to replicate in mammalian cells and to substantially integrate in a mammalian genome.

Use of the polynucleotides of the invention include their administration to a mammal as a vaccine, for therapeutic or prophylactic purposes. Such polynucleotides are used in the form of DNA as part of a plasmid that is unable to replicate in a mammalian cell and unable to integrate into the mammalian genome. Typically, such a DNA molecule is placed under the control of a promoter suitable for expression in a mammalian cell. The promoter functions either ubiquitously or tissue-specifically. Examples of non-tissue specific promoters include the early Cytomegalovirus (CMV) promoter (described in U.S. Patent No. 4,168,062) and the Rous Sarcoma Virus promoter (described in Norton & Coffin, Molec. Cell Biol. (1985) 5:281). An example of a tissue-specific promoter is the desmin promoter which drives expression in muscle cells (Li *et al.*, Gene (1989) 78:243, Li & Paulin, J. Biol. Chem. (1991) 266:6562 and Li & Paulin, J. Biol. Chem. (1993) 268:10403). Use of promoters is well-known to those skilled in the art. Useful vectors are described in numerous publications, specifically WO 94/21797 and Hartikka *et al.*, Human Gene Therapy (1996) 7:1205.

Polynucleotides of the invention which are used as a vaccine encode either a precursor or a mature form of the corresponding polypeptide. In the precursor form, the signal peptide is either homologous or heterologous. In the latter case, a eucaryotic leader sequence such as the leader sequence of the tissue-type plasminogen factor (tPA) is preferred.

As used herein, a composition of the invention contains one or several polynucleotides with optionally at least one additional polynucleotide encoding another *Chlamydia* antigen such as urease subunit A, B, or both, or a fragment, derivative, mutant, or analog thereof. The composition may also contain an

additional polynucleotide encoding a cytokine, such as interleukin-2 (IL-2) or interleukin-12 (IL-12) so that the immune response is enhanced. These additional polynucleotides are placed under appropriate control for expression. Advantageously, DNA molecules of the invention and/or additional DNA molecules to be included in the same composition, are present in the same plasmid.

Standard techniques of molecular biology for preparing and purifying polynucleotides are used in the preparation of polynucleotide therapeutics of the invention. For use as a vaccine, a polynucleotide of the invention is formulated according to various methods outlined below.

One method utilizes the polynucleotide in a naked form, free of any delivery vehicles. Such a polynucleotide is simply diluted in a physiologically acceptable solution such as sterile saline or sterile buffered saline, with or without a carrier. When present, the carrier preferably is isotonic, hypotonic, or weakly hypertonic, and has a relatively low ionic strength, such as provided by a sucrose solution, *e.g.*, a solution containing 20% sucrose.

An alternative method utilizes the polynucleotide in association with agents that assist in cellular uptake. Examples of such agents are (i) chemicals that modify cellular permeability, such as bupivacaine (see, *e.g.*, WO 94/16737), (ii) liposomes for encapsulation of the polynucleotide, or (iii) cationic lipids or silica, gold, or tungsten microparticles which associate themselves with the polynucleotides.

Anionic and neutral liposomes are well-known in the art (see, *e.g.*, Liposomes: A Practical Approach, RPC New Ed, IRL press (1990), for a detailed description of methods for making liposomes) and are useful for delivering a large range of products, including polynucleotides. Cationic lipids are also known in the art and are commonly used for gene delivery. Such

lipids include Lipofectin™ also known as DOTMA (N-[1-(2,3-dioleyloxy)propyl]-N,N,N-trimethylammonium chloride), DOTAP (1,2-bis(oleyloxy)-3-(trimethylammonio)propane), DDAB (dimethyldioctadecylammonium bromide), DOGS (dioctadecylamidologlycyl spermine) and cholesterol derivatives such as DC-Chol (3 beta-(N-(N',N'-dimethyl aminomethane)-carbamoyl) cholesterol). A description of these cationic lipids can be found in EP 187,702, WO 90/11092, U.S. Patent No. 5,283,185, WO 91/15501, WO 95/26356, and U.S. Patent No. 5,527,928. Cationic lipids for gene delivery are preferably used in association with a neutral lipid such as DOPE (dioleyl phosphatidylethanolamine), as described in WO 90/11092 as an example.

Formulation containing cationic liposomes may optionally contain other transfection-facilitating compounds. A number of them are described in WO 93/18759, WO 93/19768, WO 94/25608, and WO 95/02397. They include spermine derivatives useful for facilitating the transport of DNA through the nuclear membrane (see, for example, WO 93/18759) and membrane-permeabilizing compounds such as GALA, Gramicidine S, and cationic bile salts (see, for example, WO 93/19768).

Gold or tungsten microparticles are used for gene delivery, as described in WO 91/00359, WO 93/17706, and Tang *et al.* Nature (1992) 356:152. The microparticle-coated polynucleotide is injected *via* intradermal or intraepidermal routes using a needleless injection device ("gene gun"), such as those described in U.S. Patent No. 4,945,050, U.S. Patent No. 5,015,580, and WO 94/24263.

The amount of DNA to be used in a vaccine recipient depends, *e.g.*, on the strength of the promoter used in the DNA construct, the immunogenicity of the expressed gene product, the condition of the mammal intended for administration (*e.g.*, the weight, age, and general health of the mammal), the mode of administration, and the type of formulation. In general, a

therapeutically or prophylactically effective dose from about 1 µg to about 1 mg, preferably, from about 10 µg to about 800 µg and, more preferably, from about 25 µg to about 250 µg, can be administered to human adults. The administration can be achieved in a single dose or repeated at intervals.

The route of administration is any conventional route used in the vaccine field. As general guidance, a polynucleotide of the invention is administered *via* a mucosal surface, *e.g.*, an ocular, intranasal, pulmonary, oral, intestinal, rectal, vaginal, and urinary tract surface; or *via* a parenteral route, *e.g.*, by an intravenous, subcutaneous, intraperitoneal, intradermal, intraepidermal, or intramuscular route. The choice of administration route depends on the formulation that is selected. A polynucleotide formulated in association with bupivacaine is advantageously administered into muscles. When a neutral or anionic liposome or a cationic lipid, such as DOTMA or DC-Chol, is used, the formulation can be advantageously injected *via* intravenous, intranasal (aerosolization), intramuscular, intradermal, and subcutaneous routes. A polynucleotide in a naked form can advantageously be administered *via* the intramuscular, intradermal, or sub-cutaneous routes.

Although not absolutely required, such a composition can also contain an adjuvant. If so, a systemic adjuvant that does not require concomitant administration in order to exhibit an adjuvant effect is preferable such as, *e.g.*, QS21, which is described in U.S. Patent No. 5,057,546.

The sequence information provided in the present application enables the design of specific nucleotide probes and primers that are used for diagnostic purposes. Accordingly, a fifth aspect of the invention provides a nucleotide probe or primer having a sequence found in or derived by degeneracy of the genetic code from a sequence shown in any one of SEQ ID Nos: 1 to 10.

The term "probe" as used in the present application refers to DNA (preferably single stranded) or RNA molecules (or modifications or combinations thereof) that hybridize under the stringent conditions, as defined above, to nucleic acid molecules having SEQ ID Nos: 1 to 10 or to sequences homologous to SEQ ID Nos: 1 to 10, or to their complementary or anti-sense sequences. Generally, probes are significantly shorter than full-length sequences . Such probes contain from about 5 to about 100, preferably from about 10 to about 80, nucleotides. In particular, probes have sequences that are at least 75%, preferably at least 85%, more preferably 95% homologous to a portion of any of SEQ ID Nos: 1 to 10 or that are complementary to such sequences. Probes may contain modified bases such as inosine, methyl-5-deoxycytidine, deoxyuridine, dimethylamino-5-deoxyuridine, or diamino-2, 6-purine. Sugar or phosphate residues may also be modified or substituted. For example, a deoxyribose residue may be replaced by a polyamide (Nielsen *et al.*, Science (1991) 254:1497) and phosphate residues may be replaced by ester groups such as diphosphate, alkyl, arylphosphonate and phosphorothioate esters. In addition, the 2'-hydroxyl group on ribonucleotides may be modified by including such groups as alkyl groups.

Probes of the invention are used in diagnostic tests, as capture or detection probes. Such capture probes are conventionally immobilized on a solid support, directly or indirectly, by covalent means or by passive adsorption. A detection probe is labelled by a detection marker selected from: radioactive isotopes, enzymes such as peroxidase, alkaline phosphatase, and enzymes able to hydrolyze a chromogenic, fluorogenic, or luminescent substrate, compounds that are chromogenic, fluorogenic, or luminescent, nucleotide base analogs, and biotin.

Probes of the invention are used in any conventional hybridization technique, such as dot blot (Maniatis *et al.*,

Molecular Cloning: A Laboratory Manual (1982) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York), Southern blot (Southern, J. Mol. Biol. (1975) 98:503), northern blot (identical to Southern blot with the exception that RNA is used as a target), or the sandwich technique (Dunn *et al.*, Cell (1977) 12:23). The latter technique involves the use of a specific capture probe and/or a specific detection probe with nucleotide sequences that at least partially differ from each other.

A primer is a probe of usually about 10 to about 40 nucleotides that is used to initiate enzymatic polymerization of DNA in an amplification process (*e.g.*, PCR), in an elongation process, or in a reverse transcription method. Primers used in diagnostic methods involving PCR are labeled by methods known in the art.

As described herein, the invention also encompasses (i) a reagent comprising a probe of the invention for detecting and/or identifying the presence of *Chlamydia* in a biological material; (ii) a method for detecting and/or identifying the presence of *Chlamydia* in a biological material, in which (a) a sample is recovered or derived from the biological material, (b) DNA or RNA is extracted from the material and denatured, and (c) exposed to a probe of the invention, for example, a capture, detection probe or both, under stringent hybridization conditions, such that hybridization is detected; and (iii) a method for detecting and/or identifying the presence of *Chlamydia* in a biological material, in which (a) a sample is recovered or derived from the biological material, (b) DNA is extracted therefrom, (c) the extracted DNA is primed with at least one, and preferably two, primers of the invention and amplified by polymerase chain reaction, and (d) the amplified DNA fragment is produced.

It is apparent that disclosure of polynucleotide sequences of SEQ ID Nos: 1 to 10, their homolog, and partial

sequences of either enable their corresponding amino acid sequences. Accordingly, a sixth aspect of the invention features a substantially purified polypeptide or polypeptide derivative having an amino acid sequence encoded by a polynucleotide of the invention.

A "substantially purified polypeptide" as used herein is defined as a polypeptide that is separated from the environment in which it naturally occurs and/or that is free of the majority of the polypeptides that are present in the environment in which it was synthesized. For example, a substantially purified polypeptide is free from cytoplasmic polypeptides. Those skilled in the art would readily understand that the polypeptides of the invention may be purified from a natural source, *i.e.*, a *Chlamydia* strain, or produced by recombinant means.

Consistent with the sixth aspect of the invention are polypeptides, homologs or fragments which are modified or treated to enhance their immunogenicity in the target animal, in whom the polypeptide, homolog or fragments are intended to confer protection against Chlamydia. Such modifications or treatments include: amino acid substitutions with an amino acid derivative such as 3-methyhistidine, 4-hydroxyproline, 5-hydroxylysine etc., modifications or deletions which are carried out after preparation of the polypeptide, homolog or fragment, such as the modification of free amino, carboxyl or hydroxyl side groups of the amino acids.

Identification of homologous polypeptides or polypeptide derivatives encoded by polynucleotides of the invention which have specific antigenicity is achieved by screening for cross-reactivity with an antiserum raised against the polypeptide of reference having an amino acid sequence of any one of SEQ ID Nos: 11 to 16. The procedure is as follows: a monospecific hyperimmune antiserum is raised against a purified reference polypeptide, a fusion polypeptide (for example, an expression

product of MBP, GST, or His-tag systems), or a synthetic peptide predicted to be antigenic. Where an antiserum is raised against a fusion polypeptide, two different fusion systems are employed. Specific antigenicity can be determined according to a number of methods, including Western blot (Towbin *et al.*, Proc. Natl. Acad. Sci. USA (1979) 76:4350), dot blot, and ELISA, as described below.

In a Western blot assay, the product to be screened, either as a purified preparation or a total *E. coli* extract, is submitted to SDS-Page electrophoresis as described by Laemmli (Nature (1970) 227:680). After transfer to a nitrocellulose membrane, the material is further incubated with the monospecific hyperimmune antiserum diluted in the range of dilutions from about 1:5 to about 1:5000, preferably from about 1:100 to about 1:500. Specific antigenicity is shown once a band corresponding to the product exhibits reactivity at any of the dilutions in the above range.

In an ELISA assay, the product to be screened is preferably used as the coating antigen. A purified preparation is preferred, although a whole cell extract can also be used. Briefly, about 100 µl of a preparation at about 10 µg protein/ml are distributed into wells of a 96-well polycarbonate ELISA plate. The plate is incubated for 2 hours at 37°C then overnight at 4°C. The plate is washed with phosphate buffer saline (PBS) containing 0.05% Tween 20 (PBS/Tween buffer). The wells are saturated with 250 µl PBS containing 1% bovine serum albumin (BSA) to prevent non-specific antibody binding. After 1 hour incubation at 37°C, the plate is washed with PBS/Tween buffer. The antiserum is serially diluted in PBS/Tween buffer containing 0.5% BSA. 100 µl of dilutions are added per well. The plate is incubated for 90 minutes at 37°C, washed and evaluated according to standard procedures. For example, a goat anti-rabbit peroxidase conjugate is added to the wells when specific antibodies were raised in rabbits. Incubation is

carried out for 90 minutes at 37°C and the plate is washed. The reaction is developed with the appropriate substrate and the reaction is measured by colorimetry (absorbance measured spectrophotometrically). Under the above experimental conditions, a positive reaction is shown by O.D. values greater than a non immune control serum.

In a dot blot assay, a purified product is preferred, although a whole cell extract can also be used. Briefly, a solution of the product at about 100 µg/ml is serially two-fold diluted in 50 mM Tris-HCl (pH 7.5). 100 µl of each dilution are applied to a nitrocellulose membrane 0.45 µm set in a 96-well dot blot apparatus (Biorad). The buffer is removed by applying vacuum to the system. Wells are washed by addition of 50 mM Tris-HCl (pH 7.5) and the membrane is air-dried. The membrane is saturated in blocking buffer (50 mM Tris-HCl (pH 7.5) 0.15 M NaCl, 10 g/L skim milk) and incubated with an antiserum dilution from about 1:50 to about 1:5000, preferably about 1:500. The reaction is revealed according to standard procedures. For example, a goat anti-rabbit peroxidase conjugate is added to the wells when rabbit antibodies are used. Incubation is carried out 90 minutes at 37°C and the blot is washed. The reaction is developed with the appropriate substrate and stopped. The reaction is measured visually by the appearance of a colored spot, *e.g.*, by colorimetry. Under the above experimental conditions, a positive reaction is shown once a colored spot is associated with a dilution of at least about 1:5, preferably of at least about 1:500.

Therapeutic or prophylactic efficacy of a polypeptide or derivative of the invention can be evaluated as described below. A seventh aspect of the invention provides (i) a composition of matter comprising a polypeptide of the invention together with a diluent or carrier; specifically (ii) a pharmaceutical composition containing a therapeutically or prophylactically effective amount of a polypeptide of the invention; (iii) a

method for inducing an immune response against *Chlamydia* in a mammal, by administering to the mammal an immunogenically effective amount of a polypeptide of the invention to elicit a protective immune response to *Chlamydia*; and particularly, (iv) a method for preventing and/or treating a *Chlamydia* (*e.g.*, *C. trachomatis*. *C. psittaci*, *C. pneumoniae*. or *C. pecorum*) infection, by administering a prophylactic or therapeutic amount of a polypeptide of the invention to an infected individual. Additionally, the seventh aspect of the invention encompasses the use of a polypeptide of the invention in the preparation of a medicament for preventing and/or treating *Chlamydia* infection.

As used herein, the immunogenic compositions of the invention are administered by conventional routes known the vaccine field, in particular to a mucosal (*e.g.*, ocular, intranasal, pulmonary, oral, gastric, intestinal, rectal, vaginal, or urinary tract) surface or *via* the parenteral (*e.g.*, subcutaneous, intradermal, intramuscular, intravenous, or intraperitoneal) route. The choice of administration route depends upon a number of parameters, such as the adjuvant associated with the polypeptide. If a mucosal adjuvant is used, the intranasal or oral route is preferred. If a lipid formulation or an aluminum compound is used, the parenteral route is preferred with the sub-cutaneous or intramuscular route being most preferred. The choice also depends upon the nature of the vaccine agent. For example, a polypeptide of the invention fused to CTB or LTB is best administered to a mucosal surface.

As used herein, the composition of the invention contains one or several polypeptides or derivatives of the invention. The composition optionally contains at least one additional *Chlamydia* antigen, or a subunit, fragment, homolog, mutant, or derivative thereof.

For use in a composition of the invention, a polypeptide or derivative thereof is formulated into or with liposomes,

preferably neutral or anionic liposomes, microspheres, ISCOMS, or virus-like-particles (VLPs) to facilitate delivery and/or enhance the immune response. These compounds are readily available to one skilled in the art; for example, see Liposomes: A Practical Approach, RPC New Ed, IRL press (1990).

Adjuvants other than liposomes and the like are also used and are known in the art. Adjuvants may protect the antigen from rapid dispersal by sequestering it in a local deposit, or they may contain substances that stimulate the host to secrete factors that are chemotactic for macrophages and other components of the immune system. An appropriate selection can conventionally be made by those skilled in the art, for example, from those described below (see the eleventh aspect of the invention).

Treatment is achieved in a single dose or repeated as necessary at intervals, as can be determined readily by one skilled in the art. For example, a priming dose is followed by three booster doses at weekly or monthly intervals. An appropriate dose depends on various parameters including the recipient (*e.g.*, adult or infant), the particular vaccine antigen, the route and frequency of administration, the presence/absence or type of adjuvant, and the desired effect (*e.g.*, protection and/or treatment), as can be determined by one skilled in the art. In general, a vaccine antigen of the invention is administered by a mucosal route in an amount from about 10 µg to about 500 mg, preferably from about 1 mg to about 200 mg. For the parenteral route of administration, the dose usually does not exceed about 1 mg, preferably about 100 µg.

When used as vaccine agents, polynucleotides and polypeptides of the invention may be used sequentially as part of a multistep immunization process. For example, a mammal is initially primed with a vaccine vector of the invention such as a pox virus, *e.g.*, *via* the parenteral route, and then boosted twice with the polypeptide encoded by the vaccine vector, *e.g.*,

via the mucosal route. In another example, liposomes associated with a polypeptide or derivative of the invention is also used for priming, with boosting being carried out mucosally using a soluble polypeptide or derivative of the invention in combination with a mucosal adjuvant (*e.g.*, LT).

A polypeptide derivative of the invention is also used in accordance with the seventh aspect as a diagnostic reagent for detecting the presence of anti-*Chlamydia* antibodies, *e.g.*, in a blood sample. Such polypeptides are about 5 to about 80, preferably about 10 to about 50 amino acids in length. They are either labeled or unlabeled, depending upon the diagnostic method. Diagnostic methods involving such a reagent are described below.

Upon expression of a DNA molecule of the invention, a polypeptide or polypeptide derivative is produced and purified using known laboratory techniques. As described above, the polypeptide or polypeptide derivative may be produced as a fusion protein containing a fused tail that facilitates purification. The fusion product is used to immunize a small mammal, *e.g.*, a mouse or a rabbit, in order to raise antibodies against the polypeptide or polypeptide derivative (monospecific antibodies). Accordingly, an eighth aspect of the invention provides a monospecific antibody that binds to a polypeptide or polypeptide derivative of the invention.

By "monospecific antibody" is meant an antibody that is capable of reacting with a unique naturally-occurring *Chlamydia* polypeptide. An antibody of the invention is either polyclonal or monoclonal. Monospecific antibodies may be recombinant, *e.g.*, chimeric (*e.g.*, constituted by a variable region of murine origin associated with a human constant region), humanized (a human immunoglobulin constant backbone together with hypervariable region of animal, *e.g.*, murine, origin), and/or single chain. Both polyclonal and monospecific antibodies may also be in the form of immunoglobulin fragments, *e.g.*, F(ab)'2

or Fab fragments. The antibodies of the invention are of any isotype, *e.g.*, IgG or IgA, and polyclonal antibodies are of a single isotype or a mixture of isotypes.

Antibodies against the polypeptides, homologs or fragments of the present invention are generated by immunization of a mammal with a composition comprising said polypeptide, homolog or fragment. Scu antibodies may be polyclonal or monoclonal. Methods to produce polyclonal or monoclonal antibodies are well known in the art. For a review, see "Antibodies, A Laboratory Manual, Cold Spring Harbor Laboratory, Eds. E. Harlow and D. Lane (1988), and D.E. Yelton et al., 1981. Ann. Rev. Biochem. 50:657-680. For monoclonal antibodies, see Kohler and Milstein (1975) Nature. 256:495-497.

The antibodies of the invention, which are raised to a polypeptide or polypeptide derivative of the invention, are produced and identified using standard immunological assays, *e.g.*, Western blot analysis, dot blot assay, or ELISA (see, *e.g.*, Coligan *et al.*, Current Protocols in Immunology (1994) John Wiley & Sons, Inc., New York, NY). The antibodies are used in diagnostic methods to detect the presence of a *Chlamydia* antigen in a sample, such as a biological sample. The antibodies are also used in affinity chromatography for purifying a polypeptide or polypeptide derivative of the invention. As is discussed further below, such antibodies may be used in prophylactic and therapeutic passive immunization methods.

Accordingly, a ninth aspect of the invention provides (i) a reagent for detecting the presence of *Chlamydia* in a biological sample that contains an antibody, polypeptide, or polypeptide derivative of the invention; and (ii) a diagnostic method for detecting the presence of *Chlamydia* in a biological sample, by contacting the biological sample with an antibody, a polypeptide, or a polypeptide derivative of the invention, such that an immune complex is formed, and by detecting such complex

to indicate the presence of *Chlamydia* in the sample or the organism from which the sample is derived.

Those skilled in the art will readily understand that the immune complex is formed between a component of the sample and the antibody, polypeptide, or polypeptide derivative, whichever is used, and that any unbound material is removed prior to detecting the complex. It is understood that a polypeptide reagent is useful for detecting the presence of anti-*Chlamydia* antibodies in a sample, *e.g.*, a blood sample, while an antibody of the invention is used for screening a sample, such as a gastric extract or biopsy, for the presence of *Chlamydia* polypeptides.

For diagnostic applications, the reagent (*i.e.*, the antibody, polypeptide, or polypeptide derivative of the invention) is either in a free state or immobilized on a solid support, such as a tube, a bead, or any other conventional support used in the field. Immobilization is achieved using direct or indirect means. Direct means include passive adsorption (non-covalent binding) or covalent binding between the support and the reagent. By "indirect means" is meant that an anti-reagent compound that interacts with a reagent is first attached to the solid support. For example, if a polypeptide reagent is used, an antibody that binds to it can serve as an anti-reagent, provided that it binds to an epitope that is not involved in the recognition of antibodies in biological samples. Indirect means may also employ a ligand-receptor system, for example, where a molecule such as a vitamin is grafted onto the polypeptide reagent and the corresponding receptor immobilized on the solid phase. This is illustrated by the biotin-streptavidin system. Alternatively, a peptide tail is added chemically or by genetic engineering to the reagent and the grafted or fused product immobilized by passive adsorption or covalent linkage of the peptide tail.

Such diagnostic agents may be included in a kit which also comprises instructions for use. The reagent are labeled with a detection means which allows for the detection of the reagent when it is bound to its target. The detection means may be a fluorescent agent such as fluorescein isocyanate or fluorescein isothiocyanate, or an enzyme such as horse radish peroxidase or luciferase or alkaline phosphatase, or a radioactive element such as ^{125}I or ^{51}Cr.

Accordingly, a tenth aspect of the invention provides a process for purifying, from a biological sample, a polypeptide or polypeptide derivative of the invention, which involves carrying out antibody-based affinity chromatography with the biological sample, wherein the antibody is a monospecific antibody of the invention.

For use in a purification process of the invention, the antibody is either polyclonal or monospecific, and preferably is of the IgG type. Purified IgGs is prepared from an antiserum using standard methods (see, *e.g.*, Coligan *et al.*, Current Protocols in Immunology (1994) John Wiley & Sons, Inc., New York, NY). Conventional chromatography supports, as well as standard methods for grafting antibodies, are described in, *e.g.*, Antibodies: A Laboratory Manual, D. Lane, E. Harlow, Eds. (1988) and outlined below.

Briefly, a biological sample, such as an *C. pneumoniae* extract preferably in a buffer solution, is applied to a chromatography material, preferably equilibrated with the buffer used to dilute the biological sample so that the polypeptide or polypeptide derivative of the invention (*i.e.*, the antigen) is allowed to adsorb onto the material. The chromatography material, such as a gel or a resin coupled to an antibody of the invention, is in either a batch form or a column. The unbound components are washed off and the antigen is then eluted with an appropriate elution buffer, such as a glycine buffer or a buffer containing a chaotropic agent, *e.g.*, guanidine HCl, or high salt

concentration (*e.g.*, 3 M $MgCl_2$). Eluted fractions are recovered and the presence of the antigen is detected, *e.g.*, by measuring the absorbance at 280 nm.

An eleventh aspect of the invention provides (i) a composition of matter comprising a monospecific antibody of the invention, together with a diluent or carrier; (ii) a pharmaceutical composition comprising a therapeutically or prophylactically effective amount of a monospecific antibody of the invention, and (iii) a method for treating or preventing a *Chlamydia* (*e.g.*, *C. trachomatis, C. psittaci, C. pneumoniae or C. pecorum*) infection, by administering a therapeutic or prophylactic amount of a monospecific antibody of the invention to an infected individual. Additionally, the eleventh aspect of the invention encompasses the use of a monospecific antibody of the invention in the preparation of a medicament for treating or preventing *Chlamydia* infection.

The monospecific antibody is either polyclonal or monoclonal, preferably of the IgA isotype (predominantly). In passive immunization, the antibody is administered to a mucosal surface of a mammal, *e.g.*, the gastric mucosa, *e.g.*, orally or intragastrically, advantageously, in the presence of a bicarbonate buffer. Alternatively, systemic administration, not requiring a bicarbonate buffer, is carried out. A monospecific antibody of the invention is administered as a single active component or as a mixture with at least one monospecific antibody specific for a different *Chlamydia* polypeptide. The amount of antibody and the particular regimen used are readily determined by one skilled in the art. For example, daily administration of about 100 to 1,000 mg of antibodies over one week, or three doses per day of about 100 to 1,000 mg of antibodies over two or three days, are effective regimens for most purposes.

Therapeutic or prophylactic efficacy are evaluated using standard methods in the art, *e.g.*, by measuring induction of a

mucosal immune response or induction of protective and/or therapeutic immunity, using, *e.g.*, the C. *pneumoniae* mouse model. Those skilled in the art will readily recognize that the *C. pneumoniae* strain of the model may be replaced with another *Chlamydia* strain. For example, the efficacy of DNA molecules and polypeptides from *C. pneumoniae* is preferably evaluated in a mouse model using *C. pneumoniae* strain. Protection is determined by comparing the degree of *Chlamydia* infection to that of a control group. Protection is shown when infection is reduced by comparison to the control group. Such an evaluation is made for polynucleotides, vaccine vectors, polypeptides and derivatives thereof, as well as antibodies of the invention.

Adjuvants useful in any of the vaccine compositions described above are as follows.

Adjuvants for parenteral administration include aluminum compounds, such as aluminum hydroxide, aluminum phosphate, and aluminum hydroxy phosphate. The antigen is precipitated with, or adsorbed onto, the aluminum compound according to standard protocols. Other adjuvants, such as RIBI (ImmunoChem, Hamilton, MT), is used in parenteral administration.

Adjuvants for mucosal administration include bacterial toxins, *e.g.*, the cholera toxin (CT), the *E. coli* heat-labile toxin (LT), the *Clostridium difficile* toxin A and the *pertussis* toxin (PT), or combinations, subunits, toxoids, or mutants thereof such as a purified preparation of native cholera toxin subunit B (CTB). Fragments, homologs, derivatives, and fusions to any of these toxins are also suitable, provided that they retain adjuvant activity. Preferably, a mutant having reduced toxicity is used. Suitable mutants are described, *e.g.*, in WO 95/17211 (Arg-7-Lys CT mutant), WO 96/06627 (Arg-192-Gly LT mutant), and WO 95/34323 (Arg-9-Lys and Glu-129-Gly PT mutant). Additional LT mutants that are used in the methods and compositions of the invention include, *e.g.*, Ser-63-Lys, Ala-69-Gly, Glu-110-Asp, and Glu-112-Asp mutants. Other adjuvants,

such as a bacterial monophosphoryl lipid A (MPLA) of, *e.g.*, *E. coli*, *Salmonella minnesota*, *Salmonella typhimurium*, or *Shigella flexneri*; saponins, or polylactide glycolide (PLGA) microspheres, is also be used in mucosal administration.

Adjuvants useful for both mucosal and parenteral administrations include polyphosphazene (WO 95/02415), DC-chol (3 b-(N-(N',N'-dimethyl aminomethane)-carbamoyl) cholesterol; U.S. Patent No. 5,283,185 and WO 96/14831) and QS-21 (WO 88/09336).

Any pharmaceutical composition of the invention containing a polynucleotide, a polypeptide, a polypeptide derivative, or an antibody of the invention, is manufactured in a conventional manner. In particular, it is formulated with a pharmaceutically acceptable diluent or carrier, *e.g.*, water or a saline solution such as phosphate buffer saline. In general, a diluent or carrier is selected on the basis of the mode and route of administration, and standard pharmaceutical practice. Suitable pharmaceutical carriers or diluents, as well as pharmaceutical necessities for their use in pharmaceutical formulations, are described in *Remington's Pharmaceutical Sciences*, a standard reference text in this field and in the USP/NF.

The invention also includes methods in which *Chlamydia* infection are treated by oral administration of a *Chlamydia* polypeptide of the invention and a mucosal adjuvant, in combination with an antibiotic, an antacid, sucralfate, or a combination thereof. Examples of such compounds that can be administered with the vaccine antigen and the adjuvant are antibiotics, including, *e.g.*, macrolides, tetracyclines, and derivatives thereof (specific examples of antibiotics that can be used include azithromycin or doxicyclin or immunomodulators such as cytokines or steroids). In addition, compounds containing more than one of the above-listed components coupled together, are used. The invention also includes compositions

for carrying out these methods, *i.e.*, compositions containing a *Chlamydia* antigen (or antigens) of the invention, an adjuvant, and one or more of the above-listed compounds, in a pharmaceutically acceptable carrier or diluent.

Amounts of the above-listed compounds used in the methods and compositions of the invention are readily determined by one skilled in the art. Treatment/immunization schedules are also known and readily designed by one skilled in the art. For example, the non-vaccine components can be administered on days 1-14, and the vaccine antigen + adjuvant can be administered on days 7, 14, 21, and 28.

CLAIMS:

1. A nucleic acid molecule comprising a nucleic acid sequence which encodes a polypeptide selected from any one of:

(a) SEQ ID Nos: 12 to 16;

(b) an immunogenic fragment comprising at least 12 consecutive amino acids from a polypeptide of (a); and

(c) a polypeptide of (a) or (b) which has been modified without loss of immunogenicity, wherein said modified polypeptide is at least 75% identical in amino acid sequence to the corresponding polypeptide of (a) or (b).

2. A nucleic acid molecule comprising a nucleic acid sequence selected from any one of:

(a) SEQ ID Nos: 3 to 10;

(b) a sequence which encodes a polypeptide encoded by any one of SEQ ID Nos: 3 to 10;

(c) a sequence comprising at least 38 consecutive nucleotides from any one of the nucleic acid sequences of (a) and (b); and

(d) a sequence which encodes a polypeptide which is at least 75% identical in amino acid sequence to any one of the polypeptides encoded by SEQ ID Nos: 3 to 10.

3. A nucleic acid molecule comprising a nucleic acid sequence which is anti-sense to the nucleic acid molecule of claim 1 or 2.

4. A nucleic acid molecule comprising a nucleic acid sequence which encodes a fusion protein, said fusion protein

comprising a first polypeptide and a second polypeptide, wherein the first polypeptide is selected from any one of:

(a) SEQ ID Nos: 11-16;

(b) an immunogenic fragment comprising at least 12 consecutive amino acids from a polypeptide of SEQ ID Nos: 11-16; and

(c) a polypeptide of (a) or (b) which has been modified without loss of immunogenicity, wherein said modified polypeptide is at least 75% identical in amino acid sequence to the corresponding polypeptide of (a) or (b).

5. The nucleic acid molecule of claim 4 wherein the second polypeptide is a heterologous signal peptide.

6. The nucleic acid molecule of claim 4 wherein the second polypeptide has adjuvant activity.

7. A nucleic acid molecule according to any one of claims 1 to 6, operatively linked to one or more expression control sequences.

8. A vaccine comprising a vaccine vector and at least one first nucleic acid selected from any of:

(i) SEQ ID Nos: 1 to 10;

(ii) a nucleic acid sequence which encodes a polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(iii) a nucleic acid sequence comprising at least 38 consecutive nucleotides from any one of the nucleic acid sequences of (i) and (ii);

(iv) a nucleic acid sequence which encodes a polypeptide which is at least 75% identical in amino acid

sequence to the polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(v) a nucleic acid sequence which encodes a polypeptide whose sequence is set forth in any one of SEQ ID Nos: 11 to 16;

(vi) a nucleic acid sequence which encodes an immunogenic fragment comprising at least 12 consecutive amino acids from any one of SEQ ID Nos: 11 to 16; and

(vii) a nucleic acid sequence which encodes a polypeptide as defined in (i) to (v) or an immunogenic fragment as defined in (vi) which has been modified without loss of immunogenicity, wherein said modified polypeptide or fragment is at least 75% identical in amino acid sequence to the corresponding polypeptide of (i) to (v) or the corresponding fragment of (vi);

wherein each first nucleic acid is capable of being expressed and wherein the vaccine optionally comprises a second nucleic acid encoding and capable of expressing an additional polypeptide which enhances the immune response to the polypeptide expressed by the first nucleic acid.

9. A vaccine comprising a vaccine vector and at least one first nucleic acid encoding a fusion protein, wherein the fusion protein comprises:

(a) a first polypeptide selected from any of:

(i) a polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(ii) a polypeptide encoded by a nucleic acid sequence comprising at least 38 consecutive nucleotides from any one of SEQ ID Nos: 1 to 10;

(iii) a polypeptide which is at least 75% identical in amino acid sequence to the polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(iv) a polypeptide whose sequence is set forth in any one of SEQ ID Nos: 11 to 16;

(v) an immunogenic fragment comprising at least 12 consecutive amino acids from any one of SEQ ID Nos: 11 to 16; and

(vi) a polypeptide as defined in (i) to (iv) or an immunogenic fragment as defined in (v) which has been modified without loss of immunogenicity, wherein said modified polypeptide or fragment is at least 75% identical in amino acid sequence to the corresponding polypeptide of (i) to (iv) or the corresponding fragment of (v); and

(b) a second polypeptide;

wherein each first nucleic acid is capable of being expressed and wherein the vaccine optionally comprises a second nucleic acid encoding and capable of expressing an additional polypeptide which enhances the immune response to the first polypeptide.

10. The vaccine of claim 9 wherein the second polypeptide is a heterologous signal peptide.

11. The vaccine of claim 9 wherein the second polypeptide has adjuvant activity.

12. The vaccine of any one of claims 8 to 11 wherein wherein each first nucleic acid is operatively linked to one or more expression control sequences.

13. A vaccine comprising at least one first nucleic acid according to any one of claims 1, 2, and 4 to 7 and a vaccine

vector wherein each first nucleic acid is expressed as a polypeptide, the vaccine optionally comprising a second nucleic acid encoding an additional polypeptide which enhances the immune response to the polypeptide expressed by said first nucleic acid.

14. The vaccine of any one of claims 8 to 13 wherein the second nucleic acid encodes an additional *Chlamydia* polypeptide.

15. A pharmaceutical composition comprising a nucleic acid according to any one of claims 1 to 7 and a pharmaceutically acceptable carrier.

16. A pharmaceutical composition comprising a vaccine according to any one of claims 8 to 14 and a pharmaceutically acceptable carrier.

17. A unicellular host transformed with the nucleic acid molecule of claim 7.

18. An isolated nucleic acid probe of 5 to 100 nucleotides which hybridizes under stringent conditions to the nucleic acid molecule of any one of SEQ ID Nos: 3 to 10, or to a complementary or anti-sense sequence of said nucleic acid molecule.

19. An isolated primer of 10 to 40 nucleotides which hybridizes under stringent conditions to the nucleic acid molecules of any one of SEQ ID Nos: 3 to 10, or to a complementary or anti-sense sequence of said nucleic acid molecule.

20. A polypeptide encoded by a nucleic acid sequence according to any one of claims 1, 2 and 4 to 7.

21. A polypeptide comprising an amino acid sequence selected from any of:

(a) SEQ ID Nos: 12 to 16;

(b) an immunogenic fragment comprising at least 12 consecutive amino acids from a polypeptide of (a); and

(c) a polypeptide of (a) or (b) which has been modified without loss of immunogenicity, wherein said modified polypeptide is at least 75% identical in amino acid sequence to the corresponding polypeptide of (a) or (b).

22. A fusion polypeptide comprising a first polypeptide and a second polypeptide, wherein the first polypeptide is selected from any one of:

(a) a polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(b) a polypeptide encoded by a nucleic acid sequence comprising at least 38 consecutive nucleotides from any one of SEQ ID Nos: 1 to 10;

(c) a polypeptide which is at least 75% identical in amino acid sequence to the polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(d) a polypeptide whose sequence is set forth in any one of SEQ ID Nos: 11 to 16;

(e) an immunogenic fragment comprising at least 12 consecutive amino acids from any one of SEQ ID Nos: 11 to 16; and

(f) a polypeptide as defined in (a) to (d) or an immunogenic fragment as defined in (e) which has been modified without loss of immunogenicity, wherein said modified

polypeptide or fragment is at least 75% identical in amino acid sequence to the corresponding polypeptide of (a) to (d) or the corresponding fragment of (e).

23. The fusion protein of claim 22 wherein the second polypeptide is a heterologous signal peptide.

24. The fusion protein of claim 22 wherein the second polypeptide has adjuvant activity.

25. A method for producing a polypeptide of claim 20 or 21, or a fusion protein of any one of claims 22 to 24, comprising the step of culturing a unicellular host of claim 17.

26. An antibody against the polypeptide of claim 20 or 21, or against a fusion protein of any one of claims 22 to 24.

27. A vaccine comprising at least one first polypeptide selected from any of:

(i) a polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(ii) a polypeptide encoded by a nucleic acid sequence comprising at least 38 consecutive nucleotides from any one of SEQ ID Nos: 1 to 10;

(iii) a polypeptide which is at least 75% identical in amino acid sequence to the polypeptide encoded by any one of SEQ ID Nos: 1 to 10;

(iv) a polypeptide whose sequence is set forth in any one of SEQ ID Nos: 11 to 16;

(v) an immunogenic fragment comprising at least 12 consecutive amino acids from any one of SEQ ID Nos: 11 to 16; and

(vi) a polypeptide as defined in (i) to (iv) or an immunogenic fragment as defined in (v) which has been modified without loss of immunogenicity, wherein said modified polypeptide or fragment is at least 75% identical in amino acid sequence to the corresponding polypeptide of (i) to (iv) or the corresponding fragment of (v);

wherein the vaccine optionally comprises an additional polypeptide which enhances the immune response to the first polypeptide.

28. A vaccine comprising at least one fusion protein, wherein the fusion protein comprises:

(a) a first polypeptide selected from any of:

(i) a polypeptide encoded by SEQ ID No: 1;

(ii) a polypeptide encoded by a nucleic acid sequence comprising at least 38 consecutive nucleotides from SEQ ID No: 1;

(iii) a polypeptide which is at least 75% identical in amino acid sequence to the polypeptide encoded by SEQ ID No: 1;

(iv) a polypeptide whose sequence is set forth in SEQ ID No: 2;

(v) an immunogenic fragment comprising at least 12 consecutive amino acids from SEQ ID No:2; and

(vi) a polypeptide as defined in (i) to (iv) or an immunogenic fragment as defined in (v) which has been modified without loss of immunogenicity, wherein said modified polypeptide or fragment is at least 75% identical in amino acid sequence to the corresponding polypeptide of (i) to (iv) or the corresponding fragment of (v); and

(b) a second polypeptide;

wherein the vaccine optionally comprises an additional polypeptide which enhances the immune response to the first polypeptide.

29. The vaccine of claim 28 wherein the second polypeptide is a heterologous signal peptide.

30. The vaccine of claim 28 wherein the second polypeptide has adjuvant activity.

31. A vaccine comprising at least one first polypeptide according to any one of claims 20 to 24, optionally comprising an additional polypeptide which enhances the immune response to the first polypeptide.

32. The vaccine of any one of claims 27 to 31 wherein the additional polypeptide comprises a *Chlamydia* polypeptide.

33. A pharmaceutical composition comprising a polypeptide according to any one of claims 20 to 24 and a pharmaceutically acceptable carrier.

34. A pharmaceutical composition comprising a vaccine according to any one of claims 27 to 32 and a pharmaceutically acceptable carrier.

35. A pharmaceutical composition comprising an antibody according to claim 26 and a pharmaceutically acceptable carrier.

36. A method for preventing or treating *Chlamydia* infection using:

(a) the nucleic acid of any one of claims 1 to 7;

(b) the vaccine of any one of claims 8 to 14 and 27 to 32;

(c) the pharmaceutical composition of any one of claims 15, 16 and 33 to 35;

(d) the polypeptide of claim 20 or 21, or a fusion protein of any one of claims 22 to 24; or

(e) the antibody of claim 26.

37. A method of detecting *Chlamydia* infection comprising the step of assaying a body fluid of a mammal to be tested, with a component selected from any one of:

(a) the nucleic acid of any one of claims 1 to 7;

(b) the polypeptide of claim 20 or 21, or a fusion protein of any one of claims 22 to 24; and

(c) the antibody of claim 26.

38. A diagnostic kit comprising instructions for use and a component selected from any one of:

(a) the nucleic acid of any one of claims 1 to 7;

(b) the polypeptide of claim 20 or 21, or a fusion protein of any one of claims 22 to 24; and

(c) the antibody of claim 26.

39. A method for identifying a polypeptide of claim 20 or 21, or a fusion protein of any one of claims 22 to 24 which induces an immune response effective to prevent or lessen the severity of *Chlamydia* infection in a mammal previously immunized with polypeptide, comprising the steps of:

(a) immunizing a mouse with the polypeptide or fusion protein; and

(b) inoculating the immunized mouse with *Chlamydia;*

wherein the polypeptide or fusion protein which prevents or lessens the severity of *Chlamydia* infection in the immunized mouse compared to a non-immunized control mouse is identified.

77813-59/ccm

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

COMBINED DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that: my residence, post office address and citizenship are as stated below next to my name; that I verily believe that I am the original, first and sole inventor (if only one name is listed below) or a joint inventor (if plural inventors are named below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

CHLAMYDIA ANTIGENS AND CORRESPONDING DNA FRAGMENTS AND USES THEREOF

the specification of which

☐ is attached hereto.

☒ was filed on June 1, 2001

as U.S. Application Serial No. 09/857,128

☒ was filed on December 1, 1999

as PCT International Application No. PCT/CA99/01147

and (if applicable) was amended on December 19, 2000 and March 8, 2001

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information known to me which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §§1.56(a) and (b), which state:

"(a) A patent by its very nature is affected with a public interest. The public interest is best served, and the most effective patent examination occurs when, at the time an application is being examined, the Office is aware of and evaluates the teachings of all information material to patentability. Each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the Office, which includes a duty to disclose to the Office all information known to that individual to be material to patentability as defined in this section. The duty to disclose information exists with respect to each pending claim until the claim is cancelled or withdrawn from consideration, or the application becomes abandoned. Information material to the patentability that is cancelled or withdrawn from consideration need not be submitted if the information is not material to the patentability of any claim remaining under consideration in the application. There is no duty to submit information which is not material to the patentability of any existing claim. The duty to disclose all information known to be material to patentability is deemed to be satisfied if all information known to be material to patentability of any claim issued in a patent was cited by the Office or submitted to the Office in the manner prescribed by §§1.97(b)-(d) and 1.98. However, no patent will be granted on an application in connection with which fraud on the Office was practiced or attempted or the duty of disclosure was violated through bad faith or intentional misconduct. The Office encourages applicants to carefully examine:

(1) prior art cited in search reports of a foreign patent office in a counterpart application,

(2) the closest information over which individuals associated with the filing or prosecution of a patent application believe any pending claim patentably defines, to make sure that any material information contained therein is disclosed to the Office.

(b) Under this section, information is material to patentability when it is not cumulative to information already of record or being made of record in the application, and

(1) It establishes, by itself or in combination with other information, a prima facie case of unpatentability of a claim; or

(2) It refutes, or is inconsistent with, a position the applicant takes in:

(i) Opposing an argument of unpatentability relied on by the Office, or

(ii) Asserting an argument of patentability.

A prima facie case of unpatentability is established when the information compels a conclusion that a claim is unpatentable under the preponderance of evidence, burden-of-proof standard, giving each term in the claim its broadest reasonable construction consistent with the specification, and before any consideration is given to evidence which may be submitted in an attempt to establish a contrary conclusion of patentability."

I hereby claim foreign priority benefits under 35 United States Code, §119 and/or §365 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate filed by me or my assignee disclosing the subject matter claimed in this application and having a filing date (1) before that of the application on which priority is claimed, or (2) if no priority claimed, before the filing of this application:

PRIOR FOREIGN APPLICATION(S)

Number	Country	Filing Date *(Day/Month/Year)*	Date First Laid-open or Published	Date Patented or Granted	Priority Claimed?

I hereby claim the benefit under 35 United States Code, §119(e) of any United States provisional application(s) listed below:

Application Number	Filing Date

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56(a) which became available between the filing date of the prior application and the national or PCT international filing date of this application:

PRIOR U.S. OR PCT APPLICATION(S)

Application No.	Filing Date *(day/month/year)*	Status *(pending, abandoned, granted)*
60/110,427	01/12/98	pending
60/110,438	01/12/98	pending
60/110,339	01/12/98	pending
60/110,428	01/12/98	pending
60/110,340	01/12/98	pending

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardize the validity of the application or any patent issued thereon.

I hereby appoint the following patent agents with full power of substitution, association and revocation to prosecute this application and/or international application and to transact all business in the Patent and Trademark Office connected therewith:

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-4-

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PCT

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      4       Murdin et al.
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thereof
      8 <130> FILE REFERENCE: 77813-2
C--> 10 <140> CURRENT APPLICATION NUMBER: US/09/857,128
C--> 11 <141> CURRENT FILING DATE: 2001-10-29
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Murdin et al.

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120 125 130

gta atc aca acc ccc tca gga aaa ggt gca gtt aaa tgt gga ggg gat 547
Val Ile Thr Thr Pro Ser Gly Lys Gly Ala Val Lys Cys Gly Gly Asp
135 140 145

ctt aca ttt gat aac aat gga act att tta ttt aaa caa gat tac tgt 595
Leu Thr Phe Asp Asn Asn Gly Thr Ile Leu Phe Lys Gln Asp Tyr Cys
150 155 160 165

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gag gaa aat ggc gga gcc att tct acc aag aat ctt tct ttg aaa aac   643
Glu Glu Asn Gly Gly Ala Ile Ser Thr Lys Asn Leu Ser Leu Lys Asn
                170                 175                 180

agc acg gga tcg att tct ttt gaa ggg aat aaa tcg agc gca aca ggg   691
Ser Thr Gly Ser Ile Ser Phe Glu Gly Asn Lys Ser Ser Ala Thr Gly
            185                 190                 195

aaa aaa ggt ggg gct att tgt gct act ggt act gta gat att aca aat   739
Lys Lys Gly Gly Ala Ile Cys Ala Thr Gly Thr Val Asp Ile Thr Asn
        200                 205                 210

aat acg gct cct acc ctc ttc tcg aac aat att gct gaa gct gca ggt   787
Asn Thr Ala Pro Thr Leu Phe Ser Asn Asn Ile Ala Glu Ala Ala Gly
    215                 220                 225

gga gct ata aat agc aca gga aac tgt aca att aca ggg aat acg tct   835
Gly Ala Ile Asn Ser Thr Gly Asn Cys Thr Ile Thr Gly Asn Thr Ser
230                 235                 240                 245

ctt gta ttt tct gaa aat agt gtg aca gcg acc gca gga aat gga gga   883
Leu Val Phe Ser Glu Asn Ser Val Thr Ala Thr Ala Gly Asn Gly Gly
                250                 255                 260

gct ctt tct gga gat gcc gat gtt acc ata tct ggg aat cag agt gta   931
Ala Leu Ser Gly Asp Ala Asp Val Thr Ile Ser Gly Asn Gln Ser Val
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act ttc tca gga aac caa gct gta gct aat ggc gga gcc att tat gct   979
Thr Phe Ser Gly Asn Gln Ala Val Ala Asn Gly Gly Ala Ile Tyr Ala
        280                 285                 290

aag aag ctt aca ctg gct tcc ggg ggg ggg ggg ggg aat ccc ttt tct   1027
Lys Lys Leu Thr Leu Ala Ser Gly Gly Gly Gly Gly Asn Pro Phe Ser
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aac aat ata gtc caa ggt acc act gca ggt aat ggt gga gcc att tct   1075
Asn Asn Ile Val Gln Gly Thr Thr Ala Gly Asn Gly Gly Ala Ile Ser
310                 315                 320                 325

ata ctg gca gct gga gag tgt agt ctt ttc agc gaa gca ggg gac cat   1123
Ile Leu Ala Ala Gly Glu Cys Ser Leu Phe Ser Glu Ala Gly Asp His
                330                 335                 340

tac ctt aat ggg aat gcc att gtt gca act aca cca caa act aca aaa   1171
Tyr Leu Asn Gly Asn Ala Ile Val Ala Thr Thr Pro Gln Thr Thr Lys
            345                 350                 355

aga aat tct att gac ata gga tct act ggc aaa gat cac gaa tta cgt   1219
Arg Asn Ser Ile Asp Ile Gly Ser Thr Gly Lys Asp His Glu Leu Arg
        360                 365                 370

gca ata tct ggg cat agc atc ttt ttc tac gat ccg att act gct aat   1267
Ala Ile Ser Gly His Ser Ile Phe Phe Tyr Asp Pro Ile Thr Ala Asn
    375                 380                 385
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acg gct gcg gat tct aca gat act tta aat ctc aat aag gct gat gca   1315
Thr Ala Ala Asp Ser Thr Asp Thr Leu Asn Leu Asn Lys Ala Asp Ala
390                 395                 400                 405

ggt aat agt aca gat tat agt ggg tcg att gtt ttt tct ggt gaa aag   1363
Gly Asn Ser Thr Asp Tyr Ser Gly Ser Ile Val Phe Ser Gly Glu Lys
                410                 415                 420

ctc tct gaa gat gaa gca aaa gtt gca gac aac ctc act tct acg ctg   1411
Leu Ser Glu Asp Glu Ala Lys Val Ala Asp Asn Leu Thr Ser Thr Leu
            425                 430                 435

aag cag cct gta act cta act gca gga aat tta gta ctt aaa cgt ggt   1459
Lys Gln Pro Val Thr Leu Thr Ala Gly Asn Leu Val Leu Lys Arg Gly
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gtc act ctc gat acg aaa ggc ttt act cag acc gcg ggt tcc tct gtt   1507
Val Thr Leu Asp Thr Lys Gly Phe Thr Gln Thr Ala Gly Ser Ser Val
    455                 460                 465

att atg gat gcg ggc aca acg tta aaa gca agt aca gag gag gtc act   1555
Ile Met Asp Ala Gly Thr Thr Leu Lys Ala Ser Thr Glu Glu Val Thr
470                 475                 480                 485

tta aca ggt ctt tcc att cct gta gac tct tta ggc gag ggt aag aaa   1603
Leu Thr Gly Leu Ser Ile Pro Val Asp Ser Leu Gly Glu Gly Lys Lys
                490                 495                 500

gtt gta att gct gct tct gca gca agt aaa aat gta gcc ctt agt ggt   1651
Val Val Ile Ala Ala Ser Ala Ala Ser Lys Asn Val Ala Leu Ser Gly
            505                 510                 515

ccg att ctt ctt ttg gat aac caa ggg aat gct tat gaa aat cac gac   1699
Pro Ile Leu Leu Leu Asp Asn Gln Gly Asn Ala Tyr Glu Asn His Asp
        520                 525                 530

tta gga aaa act caa gac ttt tca ttt gtg cag ctc tct gct ctg ggt   1747
Leu Gly Lys Thr Gln Asp Phe Ser Phe Val Gln Leu Ser Ala Leu Gly
    535                 540                 545

act gca aca act aca gat gtt cca gcg gtt cct aca gta gca act cct   1795
Thr Ala Thr Thr Thr Asp Val Pro Ala Val Pro Thr Val Ala Thr Pro
550                 555                 560                 565

acg cac tat ggg tat caa ggt act tgg gga atg act tgg gtt gat gat   1843
Thr His Tyr Gly Tyr Gln Gly Thr Trp Gly Met Thr Trp Val Asp Asp
                570                 575                 580

acc gca agc act cca aag act aag aca gcg aca tta gct tgg acc aat   1891
Thr Ala Ser Thr Pro Lys Thr Lys Thr Ala Thr Leu Ala Trp Thr Asn
            585                 590                 595

aca ggc tac ctt ccg aat cct gag cgt caa gga cct tta gtt cct aat   1939
Thr Gly Tyr Leu Pro Asn Pro Glu Arg Gln Gly Pro Leu Val Pro Asn
        600                 605                 610
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agc ctt tgg gga tct ttt tca gac atc caa gcg att caa ggt gtc ata   1987
Ser Leu Trp Gly Ser Phe Ser Asp Ile Gln Ala Ile Gln Gly Val Ile
    615                 620                 625

gag aga agt gct ttg act ctt tgt tca gat cga ggc ttc tgg gct gcg   2035
Glu Arg Ser Ala Leu Thr Leu Cys Ser Asp Arg Gly Phe Trp Ala Ala
630                 635                 640                 645

gga gtc gcc aat ttc tta gat aaa gat aag aaa ggg gaa aaa cgc aaa   2083
Gly Val Ala Asn Phe Leu Asp Lys Asp Lys Lys Gly Glu Lys Arg Lys
                650                 655                 660

tac cgt cat aaa tct ggt gga tat gct atc gga ggt gca gcg caa act   2131
Tyr Arg His Lys Ser Gly Gly Tyr Ala Ile Gly Gly Ala Ala Gln Thr
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tgt tct gaa aac tta att agc ttt gcc ttt tgc caa ctc ttt ggt agc   2179
Cys Ser Glu Asn Leu Ile Ser Phe Ala Phe Cys Gln Leu Phe Gly Ser
        680                 685                 690

gat aaa gat ttc tta gtc gct aaa aat cat act gat acc tat gca gga   2227
Asp Lys Asp Phe Leu Val Ala Lys Asn His Thr Asp Thr Tyr Ala Gly
    695                 700                 705

gcc ttc tat atc caa cac att aca gaa tgt agt ggg ttc ata ggt tgt   2275
Ala Phe Tyr Ile Gln His Ile Thr Glu Cys Ser Gly Phe Ile Gly Cys
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ctc tta gat aaa ctt cct ggc tct tgg agt cat aaa ccc ctc gtt tta   2323
Leu Leu Asp Lys Leu Pro Gly Ser Trp Ser His Lys Pro Leu Val Leu
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gaa ggg cag ctc gct tat agc cac gtc agt aat gat ctg aag aca aag   2371
Glu Gly Gln Leu Ala Tyr Ser His Val Ser Asn Asp Leu Lys Thr Lys
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tat act gcg tat cct gag gtg aaa ggt tct tgg ggg aat aat gct ttt   2419
Tyr Thr Ala Tyr Pro Glu Val Lys Gly Ser Trp Gly Asn Asn Ala Phe
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aac atg atg ttg gga gct tct tct cat tct tat cct gaa tac ctg cat   2467
Asn Met Met Leu Gly Ala Ser Ser His Ser Tyr Pro Glu Tyr Leu His
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tgt ttt gat acc tat gct cca tac atc aaa ctg aat ctg acc tat ata   2515
Cys Phe Asp Thr Tyr Ala Pro Tyr Ile Lys Leu Asn Leu Thr Tyr Ile
790                 795                 800                 805

cgt cag gac agc ttc tcg gag aaa ggt aca gaa gga aga tct ttt gat   2563
Arg Gln Asp Ser Phe Ser Glu Lys Gly Thr Glu Gly Arg Ser Phe Asp
                810                 815                 820

gac agc aac ctc ttc aat tta tct ttg cct ata ggg gtg aag ttt gag   2611
Asp Ser Asn Leu Phe Asn Leu Ser Leu Pro Ile Gly Val Lys Phe Glu
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aag ttc tct gat tgt aat gac ttt tct tat gat ctg act tta tcc tat 2659
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Val Pro Asp Leu Ile Arg Asn Asp Pro Lys Cys Thr Thr Ala Leu Val
855 860 865

atc agc gga gcc tct tgg gaa act tat gcc aat aac tta gca cga cag 2755
Ile Ser Gly Ala Ser Trp Glu Thr Tyr Ala Asn Asn Leu Ala Arg Gln
870 875 880 885

gcc ttg caa gtg cgt gca ggc agt cac tac gcc ttc tct cct atg ttt 2803
Ala Leu Gln Val Arg Ala Gly Ser His Tyr Ala Phe Ser Pro Met Phe
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gaa gtg ctc ggc cag ttt gtc ttt gaa gtt cgt gga tcc tca cgg att 2851
Glu Val Leu Gly Gln Phe Val Phe Glu Val Arg Gly Ser Ser Arg Ile
905 910 915

tat aat gta gat ctt ggg ggt aag ttc caa ttc taggagcgtc tctcatgtct 2904
Tyr Asn Val Asp Leu Gly Gly Lys Phe Gln Phe
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actaacacag gcacctatac tcctaaaaat acgactactg gaatagacta tactctgaca 180
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                                            Met Lys Ser Ser Leu
                                              1               5

cat tgg ttt tta atc tcg tca tct tta gca ctt ccc ttg tca cta aat   163
His Trp Phe Leu Ile Ser Ser Ser Leu Ala Leu Pro Leu Ser Leu Asn
                  10                  15                  20

ttc tct gcg ttt gct gct gtt gtt gaa atc aat cta gga cct acc aat   211
Phe Ser Ala Phe Ala Ala Val Val Glu Ile Asn Leu Gly Pro Thr Asn
              25                  30                  35

agc ttc tct gga cca gga acc tac act cct cca gcc caa aca aca aat   259
Ser Phe Ser Gly Pro Gly Thr Tyr Thr Pro Pro Ala Gln Thr Thr Asn
          40                  45                  50
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gca gat gga act atc tat aat cta aca ggg gat gtc tca atc acc aat   307
Ala Asp Gly Thr Ile Tyr Asn Leu Thr Gly Asp Val Ser Ile Thr Asn
     55                  60                  65

gca gga tct ccg aca gct cta acc gct tcc tgc ttt aaa gaa act act   355
Ala Gly Ser Pro Thr Ala Leu Thr Ala Ser Cys Phe Lys Glu Thr Thr
 70                  75                  80                  85

ggg aat ctt tct ttc caa ggc cac ggc tac caa ttt ctc cta caa aat   403
Gly Asn Leu Ser Phe Gln Gly His Gly Tyr Gln Phe Leu Leu Gln Asn
                 90                  95                 100

atc gat gcg gga gcg aac tgt acc ttt acc aat aca gct gca aat aag   451
Ile Asp Ala Gly Ala Asn Cys Thr Phe Thr Asn Thr Ala Ala Asn Lys
            105                 110                 115

ctt ctc tcc ttt tca gga ttc tcc tat ttg tca cta ata caa acc acg   499
Leu Leu Ser Phe Ser Gly Phe Ser Tyr Leu Ser Leu Ile Gln Thr Thr
        120                 125                 130

aat gct acc aca gga aca gga gcc atc aag tcc aca gga gct tgt tct   547
Asn Ala Thr Thr Gly Thr Gly Ala Ile Lys Ser Thr Gly Ala Cys Ser
    135                 140                 145

att cag tcg aac tat agt tgc tac ttt ggc caa aac ttt tct aat gac   595
Ile Gln Ser Asn Tyr Ser Cys Tyr Phe Gly Gln Asn Phe Ser Asn Asp
150                 155                 160                 165

aat gga ggc gcc ctc caa ggc agc tct atc agt cta tcg cta aac ccc   643
Asn Gly Gly Ala Leu Gln Gly Ser Ser Ile Ser Leu Ser Leu Asn Pro
                170                 175                 180

aac cta acg ttt gcc aaa aac aaa gca acg caa aaa ggg ggt gcc ctc   691
Asn Leu Thr Phe Ala Lys Asn Lys Ala Thr Gln Lys Gly Gly Ala Leu
            185                 190                 195

tat tcc acg gga ggg att aca att aac aat acg tta aac tca gca tca   739
Tyr Ser Thr Gly Gly Ile Thr Ile Asn Asn Thr Leu Asn Ser Ala Ser
        200                 205                 210

ttt tct gaa aat acc gcg gcg aac aat ggc gga gcc att tac acg gaa   787
Phe Ser Glu Asn Thr Ala Ala Asn Asn Gly Gly Ala Ile Tyr Thr Glu
    215                 220                 225

gct agc agt ttt att agc agc aac aaa gca att agc ttt ata aac aat   835
Ala Ser Ser Phe Ile Ser Ser Asn Lys Ala Ile Ser Phe Ile Asn Asn
230                 235                 240                 245

agt gtg acc gca acc tca gct aca ggg gga gcc att tac tgt agt agt   883
Ser Val Thr Ala Thr Ser Ala Thr Gly Gly Ala Ile Tyr Cys Ser Ser
                250                 255                 260

aca tca gcc ccc aaa cca gtc tta act cta tca gac aac ggg gaa ctg   931
Thr Ser Ala Pro Lys Pro Val Leu Thr Leu Ser Asp Asn Gly Glu Leu
            265                 270                 275
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aac ttt ata gga aat aca gca att act agt ggt ggg gcg att tat act   979
Asn Phe Ile Gly Asn Thr Ala Ile Thr Ser Gly Gly Ala Ile Tyr Thr
        280                 285                 290

gac aat cta gtt ctt tct tct gga gga cct acg ctt ttt aaa aac aac   1027
Asp Asn Leu Val Leu Ser Ser Gly Gly Pro Thr Leu Phe Lys Asn Asn
    295                 300                 305

tct ggc tat gat act gca gct ccc tta gga gga gca att gcg att gct   1075
Ser Gly Tyr Asp Thr Ala Ala Pro Leu Gly Gly Ala Ile Ala Ile Ala
310                 315                 320                 325

gac tct gga tct ttg agt ctt tcg gct ctt ggt gga gac atc act ttt   1123
Asp Ser Gly Ser Leu Ser Leu Ser Ala Leu Gly Gly Asp Ile Thr Phe
                330                 335                 340

gaa gga aac aca gta gtc aaa gga gct tct tcg agt cag acc act acc   1171
Glu Gly Asn Thr Val Val Lys Gly Ala Ser Ser Ser Gln Thr Thr Thr
            345                 350                 355

aga aat tct att aac atc gga aac acc aat gct aag att gta cag ctg   1219
Arg Asn Ser Ile Asn Ile Gly Asn Thr Asn Ala Lys Ile Val Gln Leu
        360                 365                 370

cga gcc tct caa ggc aat act atc tac ttc tat gat cct ata aca act   1267
Arg Ala Ser Gln Gly Asn Thr Ile Tyr Phe Tyr Asp Pro Ile Thr Thr
    375                 380                 385

agc atc act gca gct ctc tca gat gct cta aac tta aat ggt cct gac   1315
Ser Ile Thr Ala Ala Leu Ser Asp Ala Leu Asn Leu Asn Gly Pro Asp
390                 395                 400                 405

ctt gca ggg aat cct gca tat caa gga acc atc gta ttt tct gga gag   1363
Leu Ala Gly Asn Pro Ala Tyr Gln Gly Thr Ile Val Phe Ser Gly Glu
                410                 415                 420

aag ctc tcg gaa gca gaa gct gca gaa gct gat aat ctc aaa tct aca   1411
Lys Leu Ser Glu Ala Glu Ala Ala Glu Ala Asp Asn Leu Lys Ser Thr
            425                 430                 435

att cag caa cct cta act ctt gcg gga ggg caa ctc tct ctt aaa tca   1459
Ile Gln Gln Pro Leu Thr Leu Ala Gly Gly Gln Leu Ser Leu Lys Ser
        440                 445                 450

gga gtc act cta gtt gct aag tcc ttt tcg caa tct ccg ggc tct acc   1507
Gly Val Thr Leu Val Ala Lys Ser Phe Ser Gln Ser Pro Gly Ser Thr
    455                 460                 465

ctc ctc atg gat gca ggg acc aca tta gaa acc gct gat ggg atc act   1555
Leu Leu Met Asp Ala Gly Thr Thr Leu Glu Thr Ala Asp Gly Ile Thr
470                 475                 480                 485

atc aat aat ctt gtt ctc aat gta gat tcc tta aaa gag acc aag aag   1603
Ile Asn Asn Leu Val Leu Asn Val Asp Ser Leu Lys Glu Thr Lys Lys
                490                 495                 500
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tcg ctc tct ctt gta gat cct tct gga aat gtc tac gaa gat gtc tct   1699
Ser Leu Ser Leu Val Asp Pro Ser Gly Asn Val Tyr Glu Asp Val Ser
        520                 525                 530

tgg aat aac cct caa gtc ttt tct tgt ctc act ctt act gct gac gac   1747
Trp Asn Asn Pro Gln Val Phe Ser Cys Leu Thr Leu Thr Ala Asp Asp
    535                 540                 545

ccc gcg aat att cac atc aca gac tta gct gct gat ccc cta gaa aaa   1795
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aat cct atc cat tgg gga tac caa ggg aat tgg gca tta tct tgg caa   1843
Asn Pro Ile His Trp Gly Tyr Gln Gly Asn Trp Ala Leu Ser Trp Gln
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gag gat act gcg act aaa tcc aaa gca gcg act ctt acc tgg aca aaa   1891
Glu Asp Thr Ala Thr Lys Ser Lys Ala Ala Thr Leu Thr Trp Thr Lys
            585                 590                 595

aca gga tac aat ccg aat cct gag cgt cgt gga acc tta gtt gct aac   1939
Thr Gly Tyr Asn Pro Asn Pro Glu Arg Arg Gly Thr Leu Val Ala Asn
        600                 605                 610

acg cta tgg gga tcc ttt gtt gat gtg cgc tcc ata caa cag ctt gta   1987
Thr Leu Trp Gly Ser Phe Val Asp Val Arg Ser Ile Gln Gln Leu Val
    615                 620                 625

gcc act aaa gta cgc caa tct caa gaa act cgc ggc atc tgg tgt gaa   2035
Ala Thr Lys Val Arg Gln Ser Gln Glu Thr Arg Gly Ile Trp Cys Glu
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ttt cgc cac ata agt gca ggt tat gtt gta gga gcg act aca aca tta   2131
Phe Arg His Ile Ser Ala Gly Tyr Val Val Gly Ala Thr Thr Thr Leu
            665                 670                 675

gct tct gat aat ctt atc act gca gcc ttc tgc caa tta ttc ggg aaa   2179
Ala Ser Asp Asn Leu Ile Thr Ala Ala Phe Cys Gln Leu Phe Gly Lys
        680                 685                 690

gat aga gat cac ttt ata aat aaa aat aga gct tct gcc tat gca gct   2227
Asp Arg Asp His Phe Ile Asn Lys Asn Arg Ala Ser Ala Tyr Ala Ala
    695                 700                 705

tct ctc cat ctc cag cat cta gcg acc ttg tct tct cca agc ttg tta   2275
Ser Leu His Leu Gln His Leu Ala Thr Leu Ser Ser Pro Ser Leu Leu
710                 715                 720                 725
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cgc tac ctt cct gga tct gaa agt gag cag cct gtc ctc ttt gat gct   2323
Arg Tyr Leu Pro Gly Ser Glu Ser Glu Gln Pro Val Leu Phe Asp Ala
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cag atc agc tat atc tat agt aaa aat act atg aaa acc tat tac acc   2371
Gln Ile Ser Tyr Ile Tyr Ser Lys Asn Thr Met Lys Thr Tyr Tyr Thr
            745                 750                 755

caa gca cca aag gga gag agc tcg tgg tat aat gac ggt tgc gct ctg   2419
Gln Ala Pro Lys Gly Glu Ser Ser Trp Tyr Asn Asp Gly Cys Ala Leu
        760                 765                 770

gaa ctt gcg agc tcc cta cca cac act gct tta agc cat gag ggt ctc   2467
Glu Leu Ala Ser Ser Leu Pro His Thr Ala Leu Ser His Glu Gly Leu
    775                 780                 785

ttc cac gcg tat ttt cct ttc atc aaa gta gaa gct tcg tac ata cac   2515
Phe His Ala Tyr Phe Pro Phe Ile Lys Val Glu Ala Ser Tyr Ile His
790                 795                 800                 805

caa gat agc ttc aaa gaa cgt aat act acc ttg gta cga tct ttc gat   2563
Gln Asp Ser Phe Lys Glu Arg Asn Thr Thr Leu Val Arg Ser Phe Asp
                810                 815                 820

agc ggt gat tta att aac gtc tct gtg cct att gga att acc ttc gag   2611
Ser Gly Asp Leu Ile Asn Val Ser Val Pro Ile Gly Ile Thr Phe Glu
            825                 830                 835

aga ttc tcg aga aac gag cgt gcg tct tac gaa gct act gtc atc tac   2659
Arg Phe Ser Arg Asn Glu Arg Ala Ser Tyr Glu Ala Thr Val Ile Tyr
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gtt gcc gat gtc tat cgt aag aat cct gac tgc acg aca gct ctc cta   2707
Val Ala Asp Val Tyr Arg Lys Asn Pro Asp Cys Thr Thr Ala Leu Leu
    855                 860                 865

atc aac aat acc tcg tgg aaa act aca gga acg aat ctc tca aga caa   2755
Ile Asn Asn Thr Ser Trp Lys Thr Thr Gly Thr Asn Leu Ser Arg Gln
870                 875                 880                 885

gct ggt atc gga aga gca ggg atc ttt tat gcc ttc tct cca aat ctt   2803
Ala Gly Ile Gly Arg Ala Gly Ile Phe Tyr Ala Phe Ser Pro Asn Leu
                890                 895                 900

gag gtc aca agt aac cta tct atg gaa att cgt gga tct tca cgc agc   2851
Glu Val Thr Ser Asn Leu Ser Met Glu Ile Arg Gly Ser Ser Arg Ser
            905                 910                 915

tac aat gca gat ctt gga ggt aag ttc cag ttc taaaagcgtt cctgatccct 2904
Tyr Asn Ala Asp Leu Gly Gly Lys Phe Gln Phe
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Met Lys Ile Pro Leu
1 5

cac aaa ctc ctg atc tct tcg act ctt gtc act ccc att cta ttg agc 163
His Lys Leu Leu Ile Ser Ser Thr Leu Val Thr Pro Ile Leu Leu Ser
10 15 20

att gca act tac gga gca gat gct tct tta tcc cct aca gat agc ttt 211
Ile Ala Thr Tyr Gly Ala Asp Ala Ser Leu Ser Pro Thr Asp Ser Phe
25 30 35

gat gga gcg ggc ggc tct aca ttt act cca aaa tct aca gca gat gcc 259
Asp Gly Ala Gly Gly Ser Thr Phe Thr Pro Lys Ser Thr Ala Asp Ala
40 45 50

aat gga acg aac tat gtc tta tca gga aat gtc tat ata aac gat gct 307
Asn Gly Thr Asn Tyr Val Leu Ser Gly Asn Val Tyr Ile Asn Asp Ala
55 60 65

ggg aaa ggc aca gca tta aca ggc tgc tgc ttt aca gaa act acg ggt 355
Gly Lys Gly Thr Ala Leu Thr Gly Cys Cys Phe Thr Glu Thr Thr Gly
70 75 80 85

gat ctg aca ttt act gga aag gga tac tca ttt tca ttc aac acg gta 403
Asp Leu Thr Phe Thr Gly Lys Gly Tyr Ser Phe Ser Phe Asn Thr Val
90 95 100

gat gcg ggt tcg aat gca gga gct gcg gca agc aca act gct gat aaa 451
Asp Ala Gly Ser Asn Ala Gly Ala Ala Ala Ser Thr Thr Ala Asp Lys
105 110 115

gcc cta atc ttc aca gga ttt tct aac ctt tcc ttc att gca gct cct 499
Ala Leu Ile Phe Thr Gly Phe Ser Asn Leu Ser Phe Ile Ala Ala Pro
120 125 130

gga act aca gtt gct tca gga aaa agt act tta agt tct gca gga gcc 547
Gly Thr Thr Val Ala Ser Gly Lys Ser Thr Leu Ser Ser Ala Gly Ala
135 140 145

tta aat ctt acc gat aat gga acg att ctc ttt agc caa aac gtc tcc 595
Leu Asn Leu Thr Asp Asn Gly Thr Ile Leu Phe Ser Gln Asn Val Ser
150 155 160 165

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aat gaa gct aat aac aat ggc gga gcg atc acc aca aaa act ctt tct   643
Asn Glu Ala Asn Asn Asn Gly Gly Ala Ile Thr Thr Lys Thr Leu Ser
                170                 175                 180

att tct ggg aat acc tct tct ata acc ttc act agt aat agc gca aaa   691
Ile Ser Gly Asn Thr Ser Ser Ile Thr Phe Thr Ser Asn Ser Ala Lys
            185                 190                 195

aaa tta ggt gga gcg atc tat agc tct gcg gct gca agt att tca gga   739
Lys Leu Gly Gly Ala Ile Tyr Ser Ser Ala Ala Ala Ser Ile Ser Gly
        200                 205                 210

aac acc ggc cag tta gtc ttt atg aat aat aaa gga gaa act ggg ggt   787
Asn Thr Gly Gln Leu Val Phe Met Asn Asn Lys Gly Glu Thr Gly Gly
    215                 220                 225

ggg gct ctg ggc ttt gaa gcc agc tcc tcg att act caa aat agc tcc   835
Gly Ala Leu Gly Phe Glu Ala Ser Ser Ser Ile Thr Gln Asn Ser Ser
230                 235                 240                 245

ctt ttc ttc tct gga aac act gca aca gat gct gca ggc aag ggc ggg   883
Leu Phe Phe Ser Gly Asn Thr Ala Thr Asp Ala Ala Gly Lys Gly Gly
                250                 255                 260

gcc att tat tgt gaa aaa aca gga gag act cct act ctt act atc tct   931
Ala Ile Tyr Cys Glu Lys Thr Gly Glu Thr Pro Thr Leu Thr Ile Ser
            265                 270                 275

gga aat aaa agt ctg acc ttc gcc gag aac tct tca gta act caa ggc   979
Gly Asn Lys Ser Leu Thr Phe Ala Glu Asn Ser Ser Val Thr Gln Gly
        280                 285                 290

gga gca atc tgt gcc cat ggt cta gat ctt tcc gct gct ggc cct acc   1027
Gly Ala Ile Cys Ala His Gly Leu Asp Leu Ser Ala Ala Gly Pro Thr
    295                 300                 305

cta ttt tca aat aat aga tgc ggg aac aca gct gca ggc aag ggc ggc   1075
Leu Phe Ser Asn Asn Arg Cys Gly Asn Thr Ala Ala Gly Lys Gly Gly
310                 315                 320                 325

gct att gca att gcc gac tct gga tct tta agt ctc tct gca aat caa   1123
Ala Ile Ala Ile Ala Asp Ser Gly Ser Leu Ser Leu Ser Ala Asn Gln
                330                 335                 340

gga gac atc acg ttc ctt ggc aac act cta acc tca acc tcc gcg cca   1171
Gly Asp Ile Thr Phe Leu Gly Asn Thr Leu Thr Ser Thr Ser Ala Pro
            345                 350                 355

aca tcg aca cgg aat gct atc tac ctg gga tcg tca gca aaa att acg   1219
Thr Ser Thr Arg Asn Ala Ile Tyr Leu Gly Ser Ser Ala Lys Ile Thr
        360                 365                 370

aac tta agg gca gcc caa ggc caa tct atc tat ttc tat gat ccg att   1267
Asn Leu Arg Ala Ala Gln Gly Gln Ser Ile Tyr Phe Tyr Asp Pro Ile
    375                 380                 385
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gca tct aac acc aca gga gct tca gac gtt ctg acc atc aac caa ccg   1315
Ala Ser Asn Thr Thr Gly Ala Ser Asp Val Leu Thr Ile Asn Gln Pro
390                 395                 400                 405

gat agc aac tcg cct tta gat tat tca gga acg att gta ttt tct ggg   1363
Asp Ser Asn Ser Pro Leu Asp Tyr Ser Gly Thr Ile Val Phe Ser Gly
                410                 415                 420

gaa aag ctc tct gca gat gaa gcg aaa gct gct gat aac ttc aca tct   1411
Glu Lys Leu Ser Ala Asp Glu Ala Lys Ala Ala Asp Asn Phe Thr Ser
            425                 430                 435

ata tta aag caa cca ttg gct cta gcc tct gga acc tta gca ctc aaa   1459
Ile Leu Lys Gln Pro Leu Ala Leu Ala Ser Gly Thr Leu Ala Leu Lys
        440                 445                 450

gga aat gtc gag tta gat gtc aat ggt ttc aca cag act gaa ggc tct   1507
Gly Asn Val Glu Leu Asp Val Asn Gly Phe Thr Gln Thr Glu Gly Ser
    455                 460                 465

aca ctc ctc atg caa cca gga aca aag ctc aaa gca gat act gaa gct   1555
Thr Leu Leu Met Gln Pro Gly Thr Lys Leu Lys Ala Asp Thr Glu Ala
470                 475                 480                 485

atc agt ctt acc aaa ctt gtc gtt gat ctt tct gcc tta gag gga aat   1603
Ile Ser Leu Thr Lys Leu Val Val Asp Leu Ser Ala Leu Glu Gly Asn
                490                 495                 500

aag agt gtg tcc att gaa aca gca gga gcc aac aaa act ata act cta   1651
Lys Ser Val Ser Ile Glu Thr Ala Gly Ala Asn Lys Thr Ile Thr Leu
            505                 510                 515

acc tct cct ctt gtt ttc caa gat agt agc ggc aat ttt tat gaa agc   1699
Thr Ser Pro Leu Val Phe Gln Asp Ser Ser Gly Asn Phe Tyr Glu Ser
        520                 525                 530

cat acg ata aac caa gcc ttc acg cag cct ttg gtg gta ttc act gct   1747
His Thr Ile Asn Gln Ala Phe Thr Gln Pro Leu Val Val Phe Thr Ala
    535                 540                 545

gct act gct gct agc gat att tat atc gat gcg ctt ctc act tct cca   1795
Ala Thr Ala Ala Ser Asp Ile Tyr Ile Asp Ala Leu Leu Thr Ser Pro
550                 555                 560                 565

gta caa act cca gaa cct cat tac ggg tat cag gga cat tgg gaa gcc   1843
Val Gln Thr Pro Glu Pro His Tyr Gly Tyr Gln Gly His Trp Glu Ala
                570                 575                 580

act tgg gca gac aca tca act gca aaa tca gga act atg act tgg gta   1891
Thr Trp Ala Asp Thr Ser Thr Ala Lys Ser Gly Thr Met Thr Trp Val
            585                 590                 595

act acg ggc tac aac cct aat cct gag cgt aga gct tcc gta gtt ccc   1939
Thr Thr Gly Tyr Asn Pro Asn Pro Glu Arg Arg Ala Ser Val Val Pro
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gat tca tta tgg gca tcc ttt act gac att cgc act cta cag cag atc   1987
Asp Ser Leu Trp Ala Ser Phe Thr Asp Ile Arg Thr Leu Gln Gln Ile
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atg aca tct caa gcg aat agt atc tat cag caa cga gga ctc tgg gca   2035
Met Thr Ser Gln Ala Asn Ser Ile Tyr Gln Gln Arg Gly Leu Trp Ala
630                 635                 640                 645

tca gga act gcg aat ttc ttc cat aag gat aaa tca gga act aac caa   2083
Ser Gly Thr Ala Asn Phe Phe His Lys Asp Lys Ser Gly Thr Asn Gln
                650                 655                 660

gca ttc cga cat aaa agc tac ggc tat att gtt gga gga agt gct gaa   2131
Ala Phe Arg His Lys Ser Tyr Gly Tyr Ile Val Gly Gly Ser Ala Glu
            665                 670                 675

gat ttt tct gaa aat atc ttc agt gta gct ttc tgc cag ctc ttc ggt   2179
Asp Phe Ser Glu Asn Ile Phe Ser Val Ala Phe Cys Gln Leu Phe Gly
        680                 685                 690

aaa gat aaa gac ctg ttt ata gtt gaa aat acc tct cat aac tat tta   2227
Lys Asp Lys Asp Leu Phe Ile Val Glu Asn Thr Ser His Asn Tyr Leu
    695                 700                 705

gcg tcg cta tac ctg caa cat cga gca ttc cta gga gga ctt ccc atg   2275
Ala Ser Leu Tyr Leu Gln His Arg Ala Phe Leu Gly Gly Leu Pro Met
710                 715                 720                 725

ccc tca ttt gga agt atc acc gac atg ctg aaa gat att cct ctc att   2323
Pro Ser Phe Gly Ser Ile Thr Asp Met Leu Lys Asp Ile Pro Leu Ile
                730                 735                 740

ttg aat gcc cag cta agc tac agc tac act aaa aat gat atg gat act   2371
Leu Asn Ala Gln Leu Ser Tyr Ser Tyr Thr Lys Asn Asp Met Asp Thr
            745                 750                 755

cgc tat act tcc tat cct gaa gct caa ggc tct tgg acc aat aac tct   2419
Arg Tyr Thr Ser Tyr Pro Glu Ala Gln Gly Ser Trp Thr Asn Asn Ser
        760                 765                 770

ggg gct cta gag ctc gga gga tct ctg gct cta tat ctc cct aaa gaa   2467
Gly Ala Leu Glu Leu Gly Gly Ser Leu Ala Leu Tyr Leu Pro Lys Glu
    775                 780                 785

gca ccg ttc ttc cag gga tat ttc ccc ttc tta aag ttc cag gca gtc   2515
Ala Pro Phe Phe Gln Gly Tyr Phe Pro Phe Leu Lys Phe Gln Ala Val
790                 795                 800                 805

tac agc cgc caa caa aac ttt aaa gag agt ggc gct gaa gcc cgt gct   2563
Tyr Ser Arg Gln Gln Asn Phe Lys Glu Ser Gly Ala Glu Ala Arg Ala
                810                 815                 820

ttt gat gat gga gac cta gtg aac tgc tct atc cct gtc ggc att cgg   2611
Phe Asp Asp Gly Asp Leu Val Asn Cys Ser Ile Pro Val Gly Ile Arg
            825                 830                 835
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gcc tac att ggt gat gtg tat cgt aaa aat ccc cgt tcg cgt act tct   2707
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    855                 860                 865

cta atg gtc agt gga gcc tct tgg act tcg cta tgt aaa aac ctc gca   2755
Leu Met Val Ser Gly Ala Ser Trp Thr Ser Leu Cys Lys Asn Leu Ala
870                 875                 880                 885

cga caa gcc ttc tta gca agt gct gga agc cat ctg act ctc tcc cct   2803
Arg Gln Ala Phe Leu Ala Ser Ala Gly Ser His Leu Thr Leu Ser Pro
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cat gta gaa ctc tct ggg gaa gct gct tat gag ctt cgt ggc tca gca   2851
His Val Glu Leu Ser Gly Glu Ala Ala Tyr Glu Leu Arg Gly Ser Ala
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cac atc tac aat gta gat tgt ggg cta aga tac tca ttc tagttcctac    2900
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        920                 925                 930

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ctctggctct atatctccct aaagaagcac cgttcttcca gggatatttc cccttcttaa 2400
agttccaggc agtctacagc cgccaacaaa actttaaaga gagtggcgct gaagcccgtg 2460
cttttgatga tggagaccta gtgaactgct ctatccctgt cggcattcgg ttagaaaaaa 2520
tctccgaaga tgaaaaaaat aatttcgaga tttctctagc ctacattggt gatgtgtatc 2580
gtaaaaatcc ccgttcgcgt acttctctaa tggtctcagt ggagcctctt ggacttcgct 2640
tagtaaaaac ctcgcacgac aagccttctt agcaagtgct ggaagccatc tgactctctc 2700
cctcatgtag aactctctgg ggaagctgct tatgagcttc gtggctcagc acacatctac 2760
aatgtagatt gtgggctaag atactcattc 2790

<210> 9
<211> 1100
<212> DNA
<213> Chlamydia pneumoniae

<220>
<221> CDS
<222> (101)..(979)

<400> 9
ataaagtttt ttatatgaac aaaactttga cttcattggc agacacttcg accttaacag 60

accaattttg ttgtcatccc tataaaaatc aggaattttc atg ctc tcc tca cta 115
Met Leu Ser Ser Leu
1 5

atc cgt gat tca ttt ccc ctt ctt att tta ctt ccc aca ttc cta gcg 163
Ile Arg Asp Ser Phe Pro Leu Leu Ile Leu Leu Pro Thr Phe Leu Ala
10 15 20

gca tta gga gcc tcc gta gct ggc ggc gtt atg gga acc tat atc gtt 211
Ala Leu Gly Ala Ser Val Ala Gly Gly Val Met Gly Thr Tyr Ile Val
25 30 35

gta aaa cgt att gtt tca att agt gga agt ata tct cat gca att cta 259
Val Lys Arg Ile Val Ser Ile Ser Gly Ser Ile Ser His Ala Ile Leu
40 45 50

```
gga gga att ggc ctc acc cta tgg ata caa tat aag ctt cat ctc tct   307
Gly Gly Ile Gly Leu Thr Leu Trp Ile Gln Tyr Lys Leu His Leu Ser
     55                  60                  65

ttt ttc cct atg tat gga gct att gta gga gct att ttt cta gct ctt   355
Phe Phe Pro Met Tyr Gly Ala Ile Val Gly Ala Ile Phe Leu Ala Leu
 70                  75                  80                  85

tgc atc ggc aag atc cac ctg aaa tac caa gaa agg gaa gac tct ttg   403
Cys Ile Gly Lys Ile His Leu Lys Tyr Gln Glu Arg Glu Asp Ser Leu
                 90                  95                 100

att gcg atg att tgg tct gtg ggc atg gca att gga att ata ttc att   451
Ile Ala Met Ile Trp Ser Val Gly Met Ala Ile Gly Ile Ile Phe Ile
            105                 110                 115

tcc agg ctt ccc acc ttt aat gga gag ctc atc aat ttt cta ttt ggg   499
Ser Arg Leu Pro Thr Phe Asn Gly Glu Leu Ile Asn Phe Leu Phe Gly
        120                 125                 130

aac att ctc tgg gtc acc cct tca gac ctc tat agc tta gga atc ttt   547
Asn Ile Leu Trp Val Thr Pro Ser Asp Leu Tyr Ser Leu Gly Ile Phe
    135                 140                 145

gat ctt ctt gtt tta gga att gtg gtc ctt tgc cac acc cgg ttc ctt   595
Asp Leu Leu Val Leu Gly Ile Val Val Leu Cys His Thr Arg Phe Leu
150                 155                 160                 165

gct ctt tgc ttt gat gag agg tac acg gct tta aac cat tgt tct gta   643
Ala Leu Cys Phe Asp Glu Arg Tyr Thr Ala Leu Asn His Cys Ser Val
                170                 175                 180

cag ctg tgg tat ttc cta ctt ctt gtt ctg aca gca atc acg att gtg   691
Gln Leu Trp Tyr Phe Leu Leu Leu Val Leu Thr Ala Ile Thr Ile Val
            185                 190                 195

atg ttg att tat gtg atg gga acg att ctg atg ctt agc atg ctc gtc   739
Met Leu Ile Tyr Val Met Gly Thr Ile Leu Met Leu Ser Met Leu Val
        200                 205                 210

tta cct gtt gct ata gcg tgt aga ttt tcg tac aag atg aca cga att   787
Leu Pro Val Ala Ile Ala Cys Arg Phe Ser Tyr Lys Met Thr Arg Ile
    215                 220                 225

atg ttc atc tcg gtc ctc ttg aat atc tta tgt tct ttt tct gga att   835
Met Phe Ile Ser Val Leu Leu Asn Ile Leu Cys Ser Phe Ser Gly Ile
230                 235                 240                 245

tgc atc gcc tac tgt tta gat ttc cca gta ggt cct acg ata tca ttg   883
Cys Ile Ala Tyr Cys Leu Asp Phe Pro Val Gly Pro Thr Ile Ser Leu
                250                 255                 260

ctg atg ggg tta ggt tat aca gcg agt ctt tgt gtg aag aag cgg tac   931
Leu Met Gly Leu Gly Tyr Thr Ala Ser Leu Cys Val Lys Lys Arg Tyr
            265                 270                 275
```

```
aat ccg tcg acg cct tct cct gta agt cct gaa atc aat aca aat gta   979
Asn Pro Ser Thr Pro Ser Pro Val Ser Pro Glu Ile Asn Thr Asn Val
        280                 285                 290

tagctaggga agcgcttttg gaagctttgg aggcattctt cctgttcgtc aggaagaaga 1039
tcatcaattt tatttaaagc taccagcata tctttctttt caaaatctgg ctgatgagag 1099
t                                                                 1100
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<210> 10
<211> 880
<212> DNA
<213> Chlamydiapneumoniae

<220>
<221> CDS
<222> (1)..(880)

<400> 10

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atgctctcct cactaatccg tgattcattt ccccttctta ttttacttcc cacattccta    60
gcggcattag gagcctccgt agctggcggc gttatgggaa cctatatcgt tgtaaaacgt   120
attgtttcaa ttagtggaag tatatctcat gcaattctag gaggaattgg cctcacccta   180
tggatacaat ataagcttca tctctctttt ttccctatgt atggagctat tgtaggagct   240
atttttctag ctctttgcat cggcaagatc cacctgaaat accaagaaag ggaagactct   300
ttgattgcga tgatttggtc tgtgggcatg gcaattggaa ttatattcat ttccaggctt   360
cccaccttta atggagagct catcaatttt ctatttggga acattctctg ggtcacccct   420
tcagacctct atagcttagg aatctttgat cttcttgttt taggaattgt ggtcctttgc   480
cacacccggt tccttgctct ttgctttgat gagaggtaca cggctttaaa ccattgttct   540
gtacagctgt ggtatttcct acttcttgtt ctgacagcaa tcacgattgt gatgttgatt   600
tatgtgatgg gaacgattct gatgcttagc atgctcgtct tacctgttgc tatagcgtgt   660
agattttcgt acaagatgac acgaattatg ttcatctcgg tcctcttgaa tatcttatgt   720
tctttttctg gaatttgcat cgcctactgt ttagatttcc cagtaggtcc tacgatatca   780
ttgctgatgg ggttaggtta tacagcgagt ctttgtgtag aagaagcggt acaatccgtc   840
gacgccttct cctgtaagtc ctgaaatcaa tacaaatgta                         880
```

<210> 11
<211> 928
<212> PRT
<213> Chlamydia pneumoniae

<400> 11

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Met Lys Thr Ser Ile Pro Trp Val Leu Val Ser Ser Val Leu Ala Phe
  1               5                  10                  15

Ser Cys His Leu Gln Ser Leu Ala Asn Glu Glu Leu Leu Ser Pro Asp
             20                  25                  30

Asp Ser Phe Asn Gly Asn Ile Asp Ser Gly Thr Phe Thr Pro Lys Thr
         35                  40                  45

Ser Ala Thr Thr Tyr Ser Leu Thr Gly Asp Val Phe Phe Tyr Glu Pro
     50                  55                  60

Gly Lys Gly Thr Pro Leu Ser Asp Ser Cys Phe Lys Gln Thr Thr Asp
 65                  70                  75                  80
```

```
Asn Leu Thr Phe Leu Gly Asn Gly His Ser Leu Thr Phe Gly Phe Ile
                85                  90                  95

Asp Ala Gly Thr His Ala Gly Ala Ala Ala Ser Thr Thr Ala Asn Lys
            100                 105                 110

Asn Leu Thr Phe Ser Gly Phe Ser Leu Leu Ser Phe Asp Ser Ser Pro
        115                 120                 125

Ser Thr Thr Val Thr Thr Gly Gln Gly Thr Leu Ser Ser Ala Gly Gly
    130                 135                 140

Val Asn Leu Glu Asn Ile Arg Lys Leu Val Val Ala Gly Asn Phe Ser
145                 150                 155                 160

Thr Ala Asp Gly Gly Ala Ile Lys Gly Ala Ser Phe Leu Leu Thr Gly
                165                 170                 175

Thr Ser Gly Asp Ala Leu Phe Ser Asn Asn Ser Ser Ser Thr Lys Gly
            180                 185                 190

Gly Ala Ile Ala Thr Thr Ala Gly Ala Arg Ile Ala Asn Asn Thr Gly
        195                 200                 205

Tyr Val Arg Phe Leu Ser Asn Ile Ala Ser Thr Ser Gly Gly Ala Ile
    210                 215                 220

Asp Asp Glu Gly Thr Ser Ile Leu Ser Asn Asn Lys Phe Leu Tyr Phe
225                 230                 235                 240

Glu Gly Asn Ala Ala Lys Thr Thr Gly Gly Ala Ile Cys Asn Thr Lys
                245                 250                 255

Ala Ser Gly Ser Pro Glu Leu Ile Ile Ser Asn Asn Lys Thr Leu Ile
            260                 265                 270

Phe Ala Ser Asn Val Ala Glu Thr Ser Gly Gly Ala Ile His Ala Lys
        275                 280                 285

Lys Leu Ala Leu Ser Ser Gly Gly Phe Thr Glu Phe Leu Arg Asn Asn
    290                 295                 300

Val Ser Ser Ala Thr Pro Lys Gly Gly Ala Ile Ser Ile Asp Ala Ser
305                 310                 315                 320

Gly Glu Leu Ser Leu Ser Ala Glu Thr Gly Asn Ile Thr Phe Val Arg
                325                 330                 335

Asn Thr Leu Thr Thr Thr Gly Ser Thr Asp Thr Pro Lys Arg Asn Ala
            340                 345                 350

Ile Asn Ile Gly Ser Asn Gly Lys Phe Thr Glu Leu Arg Ala Ala Lys
        355                 360                 365

Asn His Thr Ile Phe Phe Tyr Asp Pro Ile Thr Ser Glu Gly Thr Ser
    370                 375                 380
```

```
Ser Asp Val Leu Lys Ile Asn Asn Gly Ser Ala Gly Ala Leu Asn Pro
385                 390                 395                 400

Tyr Gln Gly Thr Ile Leu Phe Ser Gly Glu Thr Leu Thr Ala Asp Glu
                405                 410                 415

Leu Lys Val Ala Asp Asn Leu Lys Ser Ser Phe Thr Gln Pro Val Ser
            420                 425                 430

Leu Ser Gly Gly Lys Leu Leu Leu Gln Lys Gly Val Thr Leu Glu Ser
        435                 440                 445

Thr Ser Phe Ser Gln Glu Ala Gly Ser Leu Leu Gly Met Asp Ser Gly
    450                 455                 460

Thr Thr Leu Ser Thr Thr Ala Gly Ser Ile Thr Ile Thr Asn Leu Gly
465                 470                 475                 480

Ile Asn Val Asp Ser Leu Gly Leu Lys Gln Pro Val Ser Leu Thr Ala
                485                 490                 495

Lys Gly Ala Ser Asn Lys Val Ile Val Ser Gly Lys Leu Asn Leu Ile
            500                 505                 510

Asp Ile Glu Gly Asn Ile Tyr Glu Ser His Met Phe Ser His Asp Gln
        515                 520                 525

Leu Phe Ser Leu Leu Lys Ile Thr Val Asp Ala Asp Val Asp Thr Asn
    530                 535                 540

Val Asp Ile Ser Ser Leu Ile Pro Val Pro Ala Glu Asp Pro Asn Ser
545                 550                 555                 560

Glu Tyr Gly Phe Gln Gly Gln Trp Asn Val Asn Trp Thr Thr Asp Thr
                565                 570                 575

Ala Thr Asn Thr Lys Glu Ala Thr Ala Thr Trp Thr Lys Thr Gly Phe
            580                 585                 590

Val Pro Ser Pro Glu Arg Lys Ser Ala Leu Val Cys Asn Thr Leu Trp
        595                 600                 605

Gly Val Phe Thr Asp Ile Arg Ser Leu Gln Gln Leu Val Glu Ile Gly
    610                 615                 620

Ala Thr Gly Met Glu His Lys Gln Gly Phe Trp Val Ser Ser Met Thr
625                 630                 635                 640

Asn Phe Leu His Lys Thr Gly Asp Glu Asn Arg Lys Gly Phe Arg His
                645                 650                 655

Thr Ser Gly Gly Tyr Val Ile Gly Gly Ser Ala His Thr Pro Lys Asp
            660                 665                 670

Asp Leu Phe Thr Phe Ala Phe Cys His Leu Phe Ala Arg Asp Lys Asp
        675                 680                 685
```

Cys Phe Ile Ala His Asn Asn Ser Arg Thr Tyr Gly Gly Thr Leu Phe
690 695 700

Phe Lys His Ser His Thr Leu Gln Pro Gln Asn Tyr Leu Arg Leu Gly
705 710 715 720

Arg Ala Lys Phe Ser Glu Ser Ala Ile Glu Lys Phe Pro Arg Glu Ile
725 730 735

Pro Leu Ala Leu Asp Val Gln Val Ser Phe Ser His Ser Asp Asn Arg
740 745 750

Met Glu Thr His Tyr Thr Ser Leu Pro Glu Ser Glu Gly Ser Trp Ser
755 760 765

Asn Glu Cys Ile Ala Gly Gly Ile Gly Leu Asp Leu Pro Phe Val Leu
770 775 780

Ser Asn Pro His Pro Leu Phe Lys Thr Phe Ile Pro Gln Met Lys Val
785 790 795 800

Glu Met Val Tyr Val Ser Gln Asn Ser Phe Phe Glu Ser Ser Ser Asp
805 810 815

Gly Arg Gly Phe Ser Ile Gly Arg Leu Leu Asn Leu Ser Ile Pro Val
820 825 830

Gly Ala Lys Phe Val Gln Gly Asp Ile Gly Asp Ser Tyr Thr Tyr Asp
835 840 845

Leu Ser Gly Phe Phe Val Ser Asp Val Tyr Arg Asn Asn Pro Gln Ser
850 855 860

Thr Ala Thr Leu Val Met Ser Pro Asp Ser Trp Lys Ile Arg Gly Gly
865 870 875 880

Asn Leu Ser Arg Gln Ala Phe Leu Leu Arg Gly Ser Asn Asn Tyr Val
885 890 895

Tyr Asn Ser Asn Cys Glu Leu Phe Gly His Tyr Ala Met Glu Leu Arg
900 905 910

Gly Ser Ser Arg Asn Tyr Asn Val Asp Val Gly Thr Lys Leu Arg Phe
915 920 925

<210> 12
<211> 928
<212> PRT
<213> Chlamydia pneumoniae

<400> 12

Met Lys Ser Gln Phe
1 5

Ser Trp Leu Val Leu Ser Ser Thr Leu Ala Cys Phe Thr Ser Cys Ser
10 15 20

Thr Val Phe Ala Ala Thr Ala Glu Asn Ile Gly Pro Ser Asp Ser Phe
25 30 35

Asp Gly Ser Thr Asn Thr Gly Thr Tyr Thr Pro Lys Asn Thr Thr Thr
40 45 50

Gly Ile Asp Tyr Thr Leu Thr Gly Asp Ile Thr Leu Gln Asn Leu Gly
55 60 65

Asp Ser Ala Ala Leu Thr Lys Gly Cys Phe Ser Asp Thr Thr Glu Ser
70 75 80 85

Leu Ser Phe Ala Gly Lys Gly Tyr Ser Leu Ser Phe Leu Asn Ile Lys
90 95 100

Ser Ser Ala Glu Gly Ala Ala Leu Ser Val Thr Thr Asp Lys Asn Leu
105 110 115

Ser Leu Thr Gly Phe Ser Ser Leu Thr Phe Leu Ala Ala Pro Ser Ser
120 125 130

Val Ile Thr Thr Pro Ser Gly Lys Gly Ala Val Lys Cys Gly Gly Asp
135 140 145

Leu Thr Phe Asp Asn Asn Gly Thr Ile Leu Phe Lys Gln Asp Tyr Cys
150 155 160 165

Glu Glu Asn Gly Gly Ala Ile Ser Thr Lys Asn Leu Ser Leu Lys Asn
170 175 180

Ser Thr Gly Ser Ile Ser Phe Glu Gly Asn Lys Ser Ser Ala Thr Gly
185 190 195

Lys Lys Gly Gly Ala Ile Cys Ala Thr Gly Thr Val Asp Ile Thr Asn
200 205 210

Asn Thr Ala Pro Thr Leu Phe Ser Asn Asn Ile Ala Glu Ala Ala Gly
215 220 225

Gly Ala Ile Asn Ser Thr Gly Asn Cys Thr Ile Thr Gly Asn Thr Ser
230 235 240 245

Leu Val Phe Ser Glu Asn Ser Val Thr Ala Thr Ala Gly Asn Gly Gly
250 255 260

Ala Leu Ser Gly Asp Ala Asp Val Thr Ile Ser Gly Asn Gln Ser Val
265 270 275

Thr Phe Ser Gly Asn Gln Ala Val Ala Asn Gly Gly Ala Ile Tyr Ala
280 285 290

Lys Lys Leu Thr Leu Ala Ser Gly Gly Gly Gly Gly Asn Pro Phe Ser
295 300 305

Asn Asn Ile Val Gln Gly Thr Thr Ala Gly Asn Gly Gly Ala Ile Ser
310 315 320 325

```
Ile Leu Ala Ala Gly Glu Cys Ser Leu Phe Ser Glu Ala Gly Asp His
                330                 335                 340

Tyr Leu Asn Gly Asn Ala Ile Val Ala Thr Thr Pro Gln Thr Thr Lys
            345                 350                 355

Arg Asn Ser Ile Asp Ile Gly Ser Thr Gly Lys Asp His Glu Leu Arg
        360                 365                 370

Ala Ile Ser Gly His Ser Ile Phe Phe Tyr Asp Pro Ile Thr Ala Asn
    375                 380                 385

Thr Ala Ala Asp Ser Thr Asp Thr Leu Asn Leu Asn Lys Ala Asp Ala
390                 395                 400                 405

Gly Asn Ser Thr Asp Tyr Ser Gly Ser Ile Val Phe Ser Gly Glu Lys
                410                 415                 420

Leu Ser Glu Asp Glu Ala Lys Val Ala Asp Asn Leu Thr Ser Thr Leu
            425                 430                 435

Lys Gln Pro Val Thr Leu Thr Ala Gly Asn Leu Val Leu Lys Arg Gly
        440                 445                 450

Val Thr Leu Asp Thr Lys Gly Phe Thr Gln Thr Ala Gly Ser Ser Val
    455                 460                 465

Ile Met Asp Ala Gly Thr Thr Leu Lys Ala Ser Thr Glu Glu Val Thr
470                 475                 480                 485

Leu Thr Gly Leu Ser Ile Pro Val Asp Ser Leu Gly Glu Gly Lys Lys
                490                 495                 500

Val Val Ile Ala Ala Ser Ala Ala Ser Lys Asn Val Ala Leu Ser Gly
            505                 510                 515

Pro Ile Leu Leu Leu Asp Asn Gln Gly Asn Ala Tyr Glu Asn His Asp
        520                 525                 530

Leu Gly Lys Thr Gln Asp Phe Ser Phe Val Gln Leu Ser Ala Leu Gly
    535                 540                 545

Thr Ala Thr Thr Thr Asp Val Pro Ala Val Pro Thr Val Ala Thr Pro
550                 555                 560                 565

Thr His Tyr Gly Tyr Gln Gly Thr Trp Gly Met Thr Trp Val Asp Asp
                570                 575                 580

Thr Ala Ser Thr Pro Lys Thr Lys Thr Ala Thr Leu Ala Trp Thr Asn
            585                 590                 595

Thr Gly Tyr Leu Pro Asn Pro Glu Arg Gln Gly Pro Leu Val Pro Asn
        600                 605                 610

Ser Leu Trp Gly Ser Phe Ser Asp Ile Gln Ala Ile Gln Gly Val Ile
    615                 620                 625
```

Glu Arg Ser Ala Leu Thr Leu Cys Ser Asp Arg Gly Phe Trp Ala Ala
630 635 640 645

Gly Val Ala Asn Phe Leu Asp Lys Asp Lys Lys Gly Glu Lys Arg Lys
650 655 660

Tyr Arg His Lys Ser Gly Gly Tyr Ala Ile Gly Gly Ala Ala Gln Thr
665 670 675

Cys Ser Glu Asn Leu Ile Ser Phe Ala Phe Cys Gln Leu Phe Gly Ser
680 685 690

Asp Lys Asp Phe Leu Val Ala Lys Asn His Thr Asp Thr Tyr Ala Gly
695 700 705

Ala Phe Tyr Ile Gln His Ile Thr Glu Cys Ser Gly Phe Ile Gly Cys
710 715 720 725

Leu Leu Asp Lys Leu Pro Gly Ser Trp Ser His Lys Pro Leu Val Leu
730 735 740

Glu Gly Gln Leu Ala Tyr Ser His Val Ser Asn Asp Leu Lys Thr Lys
745 750 755

Tyr Thr Ala Tyr Pro Glu Val Lys Gly Ser Trp Gly Asn Asn Ala Phe
760 765 770

Asn Met Met Leu Gly Ala Ser Ser His Ser Tyr Pro Glu Tyr Leu His
775 780 785

Cys Phe Asp Thr Tyr Ala Pro Tyr Ile Lys Leu Asn Leu Thr Tyr Ile
790 795 800 805

Arg Gln Asp Ser Phe Ser Glu Lys Gly Thr Glu Gly Arg Ser Phe Asp
810 815 820

Asp Ser Asn Leu Phe Asn Leu Ser Leu Pro Ile Gly Val Lys Phe Glu
825 830 835

Lys Phe Ser Asp Cys Asn Asp Phe Ser Tyr Asp Leu Thr Leu Ser Tyr
840 845 850

Val Pro Asp Leu Ile Arg Asn Asp Pro Lys Cys Thr Thr Ala Leu Val
855 860 865

Ile Ser Gly Ala Ser Trp Glu Thr Tyr Ala Asn Asn Leu Ala Arg Gln
870 875 880 885

Ala Leu Gln Val Arg Ala Gly Ser His Tyr Ala Phe Ser Pro Met Phe
890 895 900

Glu Val Leu Gly Gln Phe Val Phe Glu Val Arg Gly Ser Ser Arg Ile
905 910 915

Tyr Asn Val Asp Leu Gly Gly Lys Phe Gln Phe
920 925

<210> 13
<211> 885
<212> PRT
<213> Chlamydia pneumoniae

<400> 13

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Gly Thr Tyr Thr Pro Lys Asn Thr Thr Thr Gly Ile Asp Tyr Thr Leu
  1               5                  10                  15

Thr Gly Asp Ile Thr Leu Gln Asn Leu Gly Asp Ser Ala Ala Leu Thr
            20                  25                  30

Lys Gly Cys Phe Ser Asp Thr Thr Glu Ser Leu Ser Phe Ala Gly Lys
        35                  40                  45

Gly Tyr Ser Leu Ser Phe Leu Asn Ile Lys Ser Ser Ala Glu Gly Ala
    50                  55                  60

Ala Leu Ser Val Thr Thr Asp Lys Asn Leu Ser Leu Thr Gly Phe Ser
65                  70                  75                  80

Ser Leu Thr Phe Leu Ala Ala Pro Ser Ser Val Ile Thr Thr Pro Ser
                85                  90                  95

Gly Lys Gly Ala Val Lys Cys Gly Gly Asp Leu Thr Phe Asp Asn Asn
            100                 105                 110

Gly Thr Ile Leu Phe Lys Gln Asp Tyr Cys Glu Glu Asn Gly Gly Ala
        115                 120                 125

Ile Ser Thr Lys Asn Leu Ser Leu Lys Asn Ser Thr Gly Ser Ile Ser
    130                 135                 140

Phe Glu Gly Asn Lys Ser Ser Ala Thr Gly Lys Lys Gly Gly Ala Ile
145                 150                 155                 160

Cys Ala Thr Gly Thr Val Asp Ile Thr Asn Asn Thr Ala Pro Thr Leu
                165                 170                 175

Phe Ser Asn Asn Ile Ala Glu Ala Ala Gly Gly Ala Ile Asn Ser Thr
            180                 185                 190

Gly Asn Cys Thr Ile Thr Gly Asn Thr Ser Leu Val Phe Ser Glu Asn
        195                 200                 205

Ser Val Thr Ala Thr Ala Gly Asn Gly Gly Ala Leu Ser Gly Asp Ala
    210                 215                 220

Asp Val Thr Ile Ser Gly Asn Gln Ser Val Thr Phe Ser Gly Asn Gln
225                 230                 235                 240

Ala Val Ala Asn Gly Gly Ala Ile Tyr Ala Lys Lys Leu Thr Leu Ala
                245                 250                 255

Ser Gly Gly Gly Gly Gly Asn Pro Phe Ser Asn Asn Ile Val Gln Gly
            260                 265                 270
```

```
Thr Thr Ala Gly Asn Gly Gly Ala Ile Ser Ile Leu Ala Ala Gly Glu
        275                 280                 285

Cys Ser Leu Phe Ser Glu Ala Gly Asp His Tyr Leu Asn Gly Asn Ala
    290                 295                 300

Ile Val Ala Thr Thr Pro Gln Thr Thr Lys Arg Asn Ser Ile Asp Ile
305                 310                 315                 320

Gly Ser Thr Gly Lys Asp His Glu Leu Arg Ala Ile Ser Gly His Ser
                325                 330                 335

Ile Phe Phe Tyr Asp Pro Ile Thr Ala Asn Thr Ala Ala Asp Ser Thr
            340                 345                 350

Asp Thr Leu Asn Leu Asn Lys Ala Asp Ala Gly Asn Ser Thr Asp Tyr
        355                 360                 365

Ser Gly Ser Ile Val Phe Ser Gly Glu Lys Leu Ser Glu Asp Glu Ala
    370                 375                 380

Lys Val Ala Asp Asn Leu Thr Ser Thr Leu Lys Gln Pro Val Thr Leu
385                 390                 395                 400

Thr Ala Gly Asn Leu Val Leu Lys Arg Gly Val Thr Leu Asp Thr Lys
                405                 410                 415

Gly Phe Thr Gln Thr Ala Gly Ser Ser Val Ile Met Asp Ala Gly Thr
            420                 425                 430

Thr Leu Lys Ala Ser Thr Glu Glu Val Thr Leu Thr Gly Leu Ser Ile
        435                 440                 445

Pro Val Asp Ser Leu Gly Glu Gly Lys Lys Val Val Ile Ala Ala Ser
    450                 455                 460

Ala Ala Ser Lys Asn Val Ala Leu Ser Gly Pro Ile Leu Leu Leu Asp
465                 470                 475                 480

Asn Gln Gly Asn Ala Tyr Glu Asn His Asp Leu Gly Lys Thr Gln Asp
                485                 490                 495

Phe Ser Phe Val Gln Leu Ser Ala Leu Gly Thr Ala Thr Thr Thr Asp
            500                 505                 510

Val Pro Ala Val Pro Thr Val Ala Thr Pro Thr His Tyr Gly Tyr Gln
        515                 520                 525

Gly Thr Trp Gly Met Thr Trp Val Asp Asp Thr Ala Ser Thr Pro Lys
    530                 535                 540

Thr Lys Thr Ala Thr Leu Ala Trp Thr Asn Thr Gly Tyr Leu Pro Asn
545                 550                 555                 560

Pro Glu Arg Gln Gly Pro Leu Val Pro Asn Ser Leu Trp Gly Ser Phe
                565                 570                 575
```

Ser Asp Ile Gln Ala Ile Gln Gly Val Ile Glu Arg Ser Ala Leu Thr
580 585 590

Leu Cys Ser Asp Arg Gly Phe Trp Ala Ala Gly Val Ala Asn Phe Leu
595 600 605

Asp Lys Asp Lys Lys Gly Glu Lys Arg Lys Tyr Arg His Lys Ser Gly
610 615 620

Gly Tyr Ala Ile Gly Gly Ala Ala Gln Thr Cys Ser Glu Asn Leu Ile
625 630 635 640

Ser Phe Ala Phe Cys Gln Leu Phe Gly Ser Asp Lys Asp Phe Leu Val
645 650 655

Ala Lys Asn His Thr Asp Thr Tyr Ala Gly Ala Phe Tyr Ile Gln His
660 665 670

Ile Thr Glu Cys Ser Gly Phe Ile Gly Cys Leu Leu Asp Lys Leu Pro
675 680 685

Gly Ser Trp Ser His Lys Pro Leu Val Leu Glu Gly Gln Leu Ala Tyr
690 695 700

Ser His Val Ser Asn Asp Leu Lys Thr Lys Tyr Thr Ala Tyr Pro Glu
705 710 715 720

Val Lys Gly Ser Trp Gly Asn Asn Ala Phe Asn Met Met Leu Gly Ala
725 730 735

Ser Ser His Ser Tyr Pro Glu Tyr Leu His Cys Phe Asp Thr Tyr Ala
740 745 750

Pro Tyr Ile Lys Leu Asn Leu Thr Tyr Ile Arg Gln Asp Ser Phe Ser
755 760 765

Glu Lys Gly Thr Glu Gly Arg Ser Phe Asp Asp Ser Asn Leu Phe Asn
770 775 780

Leu Ser Leu Pro Ile Gly Val Lys Phe Glu Lys Phe Ser Asp Cys Asn
785 790 795 800

Asp Phe Ser Tyr Asp Leu Thr Leu Ser Tyr Val Pro Asp Leu Ile Arg
805 810 815

Asn Asp Pro Lys Cys Thr Thr Ala Leu Val Ile Ser Gly Ala Ser Trp
820 825 830

Glu Thr Tyr Ala Asn Asn Leu Ala Arg Gln Ala Leu Gln Val Arg Ala
835 840 845

Gly Ser His Tyr Ala Phe Ser Pro Met Phe Glu Val Leu Gly Gln Phe
850 855 860

Val Phe Glu Val Arg Gly Ser Ser Arg Ile Tyr Asn Val Asp Leu Gly
865 870 875 880

Gly Lys Phe Gln Phe
885

<210> 14
<211> 928
<212> PRT
<213> Chlamydia pneumoniae

<400> 14
Met Lys Ser Ser Leu His Trp Phe Leu Ile Ser Ser Ser Leu Ala Leu
1 5 10 15

Pro Leu Ser Leu Asn Phe Ser Ala Phe Ala Ala Val Val Glu Ile Asn
20 25 30

Leu Gly Pro Thr Asn Ser Phe Ser Gly Pro Gly Thr Tyr Thr Pro Pro
35 40 45

Ala Gln Thr Thr Asn Ala Asp Gly Thr Ile Tyr Asn Leu Thr Gly Asp
50 55 60

Val Ser Ile Thr Asn Ala Gly Ser Pro Thr Ala Leu Thr Ala Ser Cys
65 70 75 80

Phe Lys Glu Thr Thr Gly Asn Leu Ser Phe Gln Gly His Gly Tyr Gln
85 90 95

Phe Leu Leu Gln Asn Ile Asp Ala Gly Ala Asn Cys Thr Phe Thr Asn
100 105 110

Thr Ala Ala Asn Lys Leu Leu Ser Phe Ser Gly Phe Ser Tyr Leu Ser
115 120 125

Leu Ile Gln Thr Thr Asn Ala Thr Thr Gly Thr Gly Ala Ile Lys Ser
130 135 140

Thr Gly Ala Cys Ser Ile Gln Ser Asn Tyr Ser Cys Tyr Phe Gly Gln
145 150 155 160

Asn Phe Ser Asn Asp Asn Gly Gly Ala Leu Gln Gly Ser Ser Ile Ser
165 170 175

Leu Ser Leu Asn Pro Asn Leu Thr Phe Ala Lys Asn Lys Ala Thr Gln
180 185 190

Lys Gly Gly Ala Leu Tyr Ser Thr Gly Gly Ile Thr Ile Asn Asn Thr
195 200 205

Leu Asn Ser Ala Ser Phe Ser Glu Asn Thr Ala Ala Asn Asn Gly Gly
210 215 220

Ala Ile Tyr Thr Glu Ala Ser Ser Phe Ile Ser Ser Asn Lys Ala Ile
225 230 235 240

Ser Phe Ile Asn Asn Ser Val Thr Ala Thr Ser Ala Thr Gly Gly Ala
245 250 255

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Ile Tyr Cys Ser Ser Thr Ser Ala Pro Lys Pro Val Leu Thr Leu Ser
            260                 265                 270

Asp Asn Gly Glu Leu Asn Phe Ile Gly Asn Thr Ala Ile Thr Ser Gly
        275                 280                 285

Gly Ala Ile Tyr Thr Asp Asn Leu Val Leu Ser Ser Gly Gly Pro Thr
    290                 295                 300

Leu Phe Lys Asn Asn Ser Gly Tyr Asp Thr Ala Ala Pro Leu Gly Gly
305                 310                 315                 320

Ala Ile Ala Ile Ala Asp Ser Gly Ser Leu Ser Leu Ser Ala Leu Gly
                325                 330                 335

Gly Asp Ile Thr Phe Glu Gly Asn Thr Val Val Lys Gly Ala Ser Ser
            340                 345                 350

Ser Gln Thr Thr Thr Arg Asn Ser Ile Asn Ile Gly Asn Thr Asn Ala
        355                 360                 365

Lys Ile Val Gln Leu Arg Ala Ser Gln Gly Asn Thr Ile Tyr Phe Tyr
    370                 375                 380

Asp Pro Ile Thr Thr Ser Ile Thr Ala Ala Leu Ser Asp Ala Leu Asn
385                 390                 395                 400

Leu Asn Gly Pro Asp Leu Ala Gly Asn Pro Ala Tyr Gln Gly Thr Ile
                405                 410                 415

Val Phe Ser Gly Glu Lys Leu Ser Glu Ala Glu Ala Ala Glu Ala Asp
            420                 425                 430

Asn Leu Lys Ser Thr Ile Gln Gln Pro Leu Thr Leu Ala Gly Gly Gln
        435                 440                 445

Leu Ser Leu Lys Ser Gly Val Thr Leu Val Ala Lys Ser Phe Ser Gln
    450                 455                 460

Ser Pro Gly Ser Thr Leu Leu Met Asp Ala Gly Thr Thr Leu Glu Thr
465                 470                 475                 480

Ala Asp Gly Ile Thr Ile Asn Asn Leu Val Leu Asn Val Asp Ser Leu
                485                 490                 495

Lys Glu Thr Lys Lys Gly Thr Leu Lys Ala Thr Gln Ala Ser Gln Thr
            500                 505                 510

Val Thr Leu Ser Gly Ser Leu Ser Leu Val Asp Pro Ser Gly Asn Val
        515                 520                 525

Tyr Glu Asp Val Ser Trp Asn Asn Pro Gln Val Phe Ser Cys Leu Thr
    530                 535                 540

Leu Thr Ala Asp Asp Pro Ala Asn Ile His Ile Thr Asp Leu Ala Ala
545                 550                 555                 560
```

```
Asp Pro Leu Glu Lys Asn Pro Ile His Trp Gly Tyr Gln Gly Asn Trp
                565                 570                 575

Ala Leu Ser Trp Gln Glu Asp Thr Ala Thr Lys Ser Lys Ala Ala Thr
            580                 585                 590

Leu Thr Trp Thr Lys Thr Gly Tyr Asn Pro Asn Pro Glu Arg Arg Gly
        595                 600                 605

Thr Leu Val Ala Asn Thr Leu Trp Gly Ser Phe Val Asp Val Arg Ser
    610                 615                 620

Ile Gln Gln Leu Val Ala Thr Lys Val Arg Gln Ser Gln Glu Thr Arg
625                 630                 635                 640

Gly Ile Trp Cys Glu Gly Ile Ser Asn Phe Phe His Lys Asp Ser Thr
                645                 650                 655

Lys Ile Asn Lys Gly Phe Arg His Ile Ser Ala Gly Tyr Val Val Gly
            660                 665                 670

Ala Thr Thr Thr Leu Ala Ser Asp Asn Leu Ile Thr Ala Ala Phe Cys
        675                 680                 685

Gln Leu Phe Gly Lys Asp Arg Asp His Phe Ile Asn Lys Asn Arg Ala
    690                 695                 700

Ser Ala Tyr Ala Ala Ser Leu His Leu Gln His Leu Ala Thr Leu Ser
705                 710                 715                 720

Ser Pro Ser Leu Leu Arg Tyr Leu Pro Gly Ser Glu Ser Glu Gln Pro
                725                 730                 735

Val Leu Phe Asp Ala Gln Ile Ser Tyr Ile Tyr Ser Lys Asn Thr Met
            740                 745                 750

Lys Thr Tyr Tyr Thr Gln Ala Pro Lys Gly Glu Ser Ser Trp Tyr Asn
        755                 760                 765

Asp Gly Cys Ala Leu Glu Leu Ala Ser Ser Leu Pro His Thr Ala Leu
    770                 775                 780

Ser His Glu Gly Leu Phe His Ala Tyr Phe Pro Phe Ile Lys Val Glu
785                 790                 795                 800

Ala Ser Tyr Ile His Gln Asp Ser Phe Lys Glu Arg Asn Thr Thr Leu
                805                 810                 815

Val Arg Ser Phe Asp Ser Gly Asp Leu Ile Asn Val Ser Val Pro Ile
            820                 825                 830

Gly Ile Thr Phe Glu Arg Phe Ser Arg Asn Glu Arg Ala Ser Tyr Glu
        835                 840                 845

Ala Thr Val Ile Tyr Val Ala Asp Val Tyr Arg Lys Asn Pro Asp Cys
    850                 855                 860
```

```
Thr Thr Ala Leu Leu Ile Asn Asn Thr Ser Trp Lys Thr Thr Gly Thr
865                 870                 875                 880

Asn Leu Ser Arg Gln Ala Gly Ile Gly Arg Ala Gly Ile Phe Tyr Ala
                885                 890                 895

Phe Ser Pro Asn Leu Glu Val Thr Ser Asn Leu Ser Met Glu Ile Arg
            900                 905                 910

Gly Ser Ser Arg Ser Tyr Asn Ala Asp Leu Gly Gly Lys Phe Gln Phe
        915                 920                 925
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<210> 15
<211> 930
<212> PRT
<213> Chlamydia pneumoniae

<400> 15

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Met Lys Ile Pro Leu His Lys Leu Leu Ile Ser Ser Thr Leu Val Thr
  1               5                  10                  15

Pro Ile Leu Leu Ser Ile Ala Thr Tyr Gly Ala Asp Ala Ser Leu Ser
            20                  25                  30

Pro Thr Asp Ser Phe Asp Gly Ala Gly Gly Ser Thr Phe Thr Pro Lys
        35                  40                  45

Ser Thr Ala Asp Ala Asn Gly Thr Asn Tyr Val Leu Ser Gly Asn Val
    50                  55                  60

Tyr Ile Asn Asp Ala Gly Lys Gly Thr Ala Leu Thr Gly Cys Cys Phe
65                  70                  75                  80

Thr Glu Thr Thr Gly Asp Leu Thr Phe Thr Gly Lys Gly Tyr Ser Phe
                85                  90                  95

Ser Phe Asn Thr Val Asp Ala Gly Ser Asn Ala Gly Ala Ala Ala Ser
            100                 105                 110

Thr Thr Ala Asp Lys Ala Leu Ile Phe Thr Gly Phe Ser Asn Leu Ser
        115                 120                 125

Phe Ile Ala Ala Pro Gly Thr Thr Val Ala Ser Gly Lys Ser Thr Leu
    130                 135                 140

Ser Ser Ala Gly Ala Leu Asn Leu Thr Asp Asn Gly Thr Ile Leu Phe
145                 150                 155                 160

Ser Gln Asn Val Ser Asn Glu Ala Asn Asn Asn Gly Gly Ala Ile Thr
                165                 170                 175

Thr Lys Thr Leu Ser Ile Ser Gly Asn Thr Ser Ser Ile Thr Phe Thr
            180                 185                 190

Ser Asn Ser Ala Lys Lys Leu Gly Gly Ala Ile Tyr Ser Ser Ala Ala
        195                 200                 205
```

```
Ala Ser Ile Ser Gly Asn Thr Gly Gln Leu Val Phe Met Asn Asn Lys
    210                 215                 220

Gly Glu Thr Gly Gly Gly Ala Leu Gly Phe Glu Ala Ser Ser Ser Ile
225                 230                 235                 240

Thr Gln Asn Ser Ser Leu Phe Phe Ser Gly Asn Thr Ala Thr Asp Ala
                245                 250                 255

Ala Gly Lys Gly Gly Ala Ile Tyr Cys Glu Lys Thr Gly Glu Thr Pro
            260                 265                 270

Thr Leu Thr Ile Ser Gly Asn Lys Ser Leu Thr Phe Ala Glu Asn Ser
        275                 280                 285

Ser Val Thr Gln Gly Gly Ala Ile Cys Ala His Gly Leu Asp Leu Ser
    290                 295                 300

Ala Ala Gly Pro Thr Leu Phe Ser Asn Asn Arg Cys Gly Asn Thr Ala
305                 310                 315                 320

Ala Gly Lys Gly Gly Ala Ile Ala Ile Ala Asp Ser Gly Ser Leu Ser
                325                 330                 335

Leu Ser Ala Asn Gln Gly Asp Ile Thr Phe Leu Gly Asn Thr Leu Thr
            340                 345                 350

Ser Thr Ser Ala Pro Thr Ser Thr Arg Asn Ala Ile Tyr Leu Gly Ser
        355                 360                 365

Ser Ala Lys Ile Thr Asn Leu Arg Ala Ala Gln Gly Gln Ser Ile Tyr
    370                 375                 380

Phe Tyr Asp Pro Ile Ala Ser Asn Thr Thr Gly Ala Ser Asp Val Leu
385                 390                 395                 400

Thr Ile Asn Gln Pro Asp Ser Asn Ser Pro Leu Asp Tyr Ser Gly Thr
                405                 410                 415

Ile Val Phe Ser Gly Glu Lys Leu Ser Ala Asp Glu Ala Lys Ala Ala
            420                 425                 430

Asp Asn Phe Thr Ser Ile Leu Lys Gln Pro Leu Ala Leu Ala Ser Gly
        435                 440                 445

Thr Leu Ala Leu Lys Gly Asn Val Glu Leu Asp Val Asn Gly Phe Thr
    450                 455                 460

Gln Thr Glu Gly Ser Thr Leu Leu Met Gln Pro Gly Thr Lys Leu Lys
465                 470                 475                 480

Ala Asp Thr Glu Ala Ile Ser Leu Thr Lys Leu Val Val Asp Leu Ser
                485                 490                 495

Ala Leu Glu Gly Asn Lys Ser Val Ser Ile Glu Thr Ala Gly Ala Asn
            500                 505                 510
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Lys Thr Ile Thr Leu Thr Ser Pro Leu Val Phe Gln Asp Ser Ser Gly
515 520 525

Asn Phe Tyr Glu Ser His Thr Ile Asn Gln Ala Phe Thr Gln Pro Leu
530 535 540

Val Val Phe Thr Ala Ala Thr Ala Ala Ser Asp Ile Tyr Ile Asp Ala
545 550 555 560

Leu Leu Thr Ser Pro Val Gln Thr Pro Glu Pro His Tyr Gly Tyr Gln
565 570 575

Gly His Trp Glu Ala Thr Trp Ala Asp Thr Ser Thr Ala Lys Ser Gly
580 585 590

Thr Met Thr Trp Val Thr Thr Gly Tyr Asn Pro Asn Pro Glu Arg Arg
595 600 605

Ala Ser Val Val Pro Asp Ser Leu Trp Ala Ser Phe Thr Asp Ile Arg
610 615 620

Thr Leu Gln Gln Ile Met Thr Ser Gln Ala Asn Ser Ile Tyr Gln Gln
625 630 635 640

Arg Gly Leu Trp Ala Ser Gly Thr Ala Asn Phe Phe His Lys Asp Lys
645 650 655

Ser Gly Thr Asn Gln Ala Phe Arg His Lys Ser Tyr Gly Tyr Ile Val
660 665 670

Gly Gly Ser Ala Glu Asp Phe Ser Glu Asn Ile Phe Ser Val Ala Phe
675 680 685

Cys Gln Leu Phe Gly Lys Asp Lys Asp Leu Phe Ile Val Glu Asn Thr
690 695 700

Ser His Asn Tyr Leu Ala Ser Leu Tyr Leu Gln His Arg Ala Phe Leu
705 710 715 720

Gly Gly Leu Pro Met Pro Ser Phe Gly Ser Ile Thr Asp Met Leu Lys
725 730 735

Asp Ile Pro Leu Ile Leu Asn Ala Gln Leu Ser Tyr Ser Tyr Thr Lys
740 745 750

Asn Asp Met Asp Thr Arg Tyr Thr Ser Tyr Pro Glu Ala Gln Gly Ser
755 760 765

Trp Thr Asn Asn Ser Gly Ala Leu Glu Leu Gly Gly Ser Leu Ala Leu
770 775 780

Tyr Leu Pro Lys Glu Ala Pro Phe Phe Gln Gly Tyr Phe Pro Phe Leu
785 790 795 800

Lys Phe Gln Ala Val Tyr Ser Arg Gln Gln Asn Phe Lys Glu Ser Gly
805 810 815

Ala Glu Ala Arg Ala Phe Asp Asp Gly Asp Leu Val Asn Cys Ser Ile
820 825 830

Pro Val Gly Ile Arg Leu Glu Lys Ile Ser Glu Asp Glu Lys Asn Asn
835 840 845

Phe Glu Ile Ser Leu Ala Tyr Ile Gly Asp Val Tyr Arg Lys Asn Pro
850 855 860

Arg Ser Arg Thr Ser Leu Met Val Ser Gly Ala Ser Trp Thr Ser Leu
865 870 875 880

Cys Lys Asn Leu Ala Arg Gln Ala Phe Leu Ala Ser Ala Gly Ser His
885 890 895

Leu Thr Leu Ser Pro His Val Glu Leu Ser Gly Glu Ala Ala Tyr Glu
900 905 910

Leu Arg Gly Ser Ala His Ile Tyr Asn Val Asp Cys Gly Leu Arg Tyr
915 920 925

Ser Phe
930

<210> 16
<211> 293
<212> PRT
<213> Chlamydia pneumoniae

<400> 16
Met Leu Ser Ser Leu Ile Arg Asp Ser Phe Pro Leu Leu Ile Leu Leu
1 5 10 15

Pro Thr Phe Leu Ala Ala Leu Gly Ala Ser Val Ala Gly Gly Val Met
20 25 30

Gly Thr Tyr Ile Val Val Lys Arg Ile Val Ser Ile Ser Gly Ser Ile
35 40 45

Ser His Ala Ile Leu Gly Gly Ile Gly Leu Thr Leu Trp Ile Gln Tyr
50 55 60

Lys Leu His Leu Ser Phe Phe Pro Met Tyr Gly Ala Ile Val Gly Ala
65 70 75 80

Ile Phe Leu Ala Leu Cys Ile Gly Lys Ile His Leu Lys Tyr Gln Glu
85 90 95

Arg Glu Asp Ser Leu Ile Ala Met Ile Trp Ser Val Gly Met Ala Ile
100 105 110

Gly Ile Ile Phe Ile Ser Arg Leu Pro Thr Phe Asn Gly Glu Leu Ile
115 120 125

Asn Phe Leu Phe Gly Asn Ile Leu Trp Val Thr Pro Ser Asp Leu Tyr
130 135 140

```
Ser Leu Gly Ile Phe Asp Leu Leu Val Leu Gly Ile Val Val Leu Cys
145                 150                 155                 160

His Thr Arg Phe Leu Ala Leu Cys Phe Asp Glu Arg Tyr Thr Ala Leu
                165                 170                 175

Asn His Cys Ser Val Gln Leu Trp Tyr Phe Leu Leu Leu Val Leu Thr
            180                 185                 190

Ala Ile Thr Ile Val Met Leu Ile Tyr Val Met Gly Thr Ile Leu Met
        195                 200                 205

Leu Ser Met Leu Val Leu Pro Val Ala Ile Ala Cys Arg Phe Ser Tyr
    210                 215                 220

Lys Met Thr Arg Ile Met Phe Ile Ser Val Leu Leu Asn Ile Leu Cys
225                 230                 235                 240

Ser Phe Ser Gly Ile Cys Ile Ala Tyr Cys Leu Asp Phe Pro Val Gly
                245                 250                 255

Pro Thr Ile Ser Leu Leu Met Gly Leu Gly Tyr Thr Ala Ser Leu Cys
            260                 265                 270

Val Lys Lys Arg Tyr Asn Pro Ser Thr Pro Ser Pro Val Ser Pro Glu
        275                 280                 285

Ile Asn Thr Asn Val
    290
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<210> 17
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> T-cell epitope

<400> 17
Arg Leu Leu Asn Leu Ser Ile Pro Val
5

<210> 18
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> B-cell epitope

<400> 18
His Lys Thr Gly Asp Glu Asn Arg Lys Gly Phe Arg His Thr Ser
5   10   15

<210> 19
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> T-cell epitope

<400> 19
Val Leu Gly Gln Phe Val Phe
5

<210> 20
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> B-cell epitope

<400> 20
Asp Lys Asp Lys Lys Gly Glu Lys Arg Lys Tyr Arg His Lys Ser Gly
5 10 15

<210> 21
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> T-cell epitope

<400> 21
Thr Leu Trp Gly Ser Phe Val Asp Val
5

<210> 22
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> B-cell epitope

<400> 22
Trp Thr Lys Thr Gly Tyr Asn Pro Asn Pro Glu Arg Arg Gly
5 10

<210> 23
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> T-cell epitope

<400> 23
Lys Leu Leu Ile Ser Ser Thr Leu Val
5

<210> 24
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> B-cell epitope

<400> 24
Glu Lys Ile Ser Glu Asp Glu Lys Asn Asn Phe
5 10

<210> 25
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> B-cell epitope

<400> 25
Tyr Arg Lys Asn Pro Arg Ser Arg Thr
5

<210> 26
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> T-cell epitope

<400> 26
Phe Leu Phe Gly Asn Ile Leu Trp Val
5

<210> 27
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> B-cell epitope

<400> 27
His Leu Lys Tyr Gln Glu Arg Glu Asp Ser
5 10

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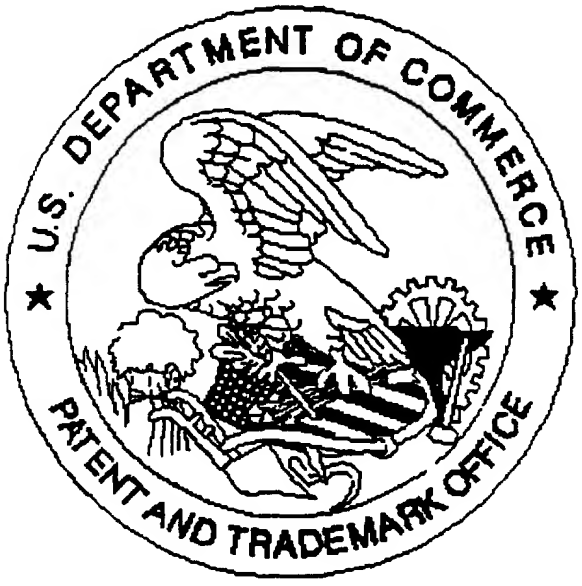

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☑ Page(s) 1 of 1 of Sequence listing were not present for scanning. (Document title)

☐ Page(s)_____ of _____ were not present for scanning. (Document title)

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